

TUFTSCOPE

THE INTERDISCIPLINARY JOURNAL OF
HEALTH, ETHICS, AND POLICY



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The Future of Medical Imaging

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Since 2001 *TuftsScope: The Interdisciplinary Journal of Health, Ethics, & Policy*, has provided an academic forum for discussion of pertinent healthcare and biosocial issues in today's world. The journal addresses different aspects of healthcare, bioethics, public health, policy, and active citizenship. It is operated and edited by undergraduate students of Tufts University and is advised by an Editorial Board composed of Tufts undergraduates and faculty. Today the journal is one of the few peer reviewed undergraduate published journals in the country.

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Celia Begel and Dr. Steven Kaminsky.*

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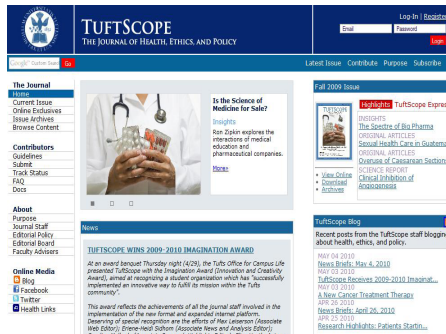
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Cover Image: In this issue *TuftScope* explores the future of medical imaging and communication.

Image Credit: *Luislouro*

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TuftsScope Online Exclusives

Accompanying this issue we offer several *TuftsScope Online Exclusives*. In this special section we provide a summary of the content readers will find online:

Orphan Drug Act: Boris Gites et al. discuss the economic and policy repercussions of the Orphan Drug Act of 1983. The effects of the Act on encouraging research into pharmaceuticals for rare diseases and financial repercussions for the pharmaceutical industry are detailed.

Technology and Public Health: There is a fine balance to be achieved in funding basic science for the future versus measures for today. Irene Swanenberg argues that a careful reevaluation of the prioritization of biomedical investments into public health is necessary.

Ethics of Gamete Donation: Tuua Ruutiainen considers the ethics of disclosure regarding gamete donation and addresses the question: to what extent should parental interests be weighed against the rights of children to know their biological origin?

Sexual Health in Taiwan: An unwillingness to discuss issues of sexual health in Taiwan has resulted in serious public health concerns. Teresa Lii offers a context for these developments and gauges the potential for the liberalization of sexual health policies.

Transgender Perspectives: In a special commentary Julie Sayre evaluates the specific challenges facing members of the transgender community with regards to receiving adequate medical care.

LETTER FROM THE EDITOR

Transition at the Scope

Dear Reader,

The Spring 2010 issue coincides with a time of transition: both the implementation of a new platform for *TuftScope* and the culmination of sweeping US healthcare reform. As anticipated after the fall 2008 election, though arguably overshadowed by more than a year of acrimonious public and political debate, President Barack Obama signed the Patient Protection and Affordable Care Act into law on March 23rd. However, in the lukewarm wake of this legislative reform package (a number of whose stipulations are delayed as far into the future as 2018) remain still ongoing reforms: the ever-present spread of accessible technologies, a newfound sensitivity to best-practices in medicine, and the inexorable outpour of scientific findings as well as academic reconsiderations of health solutions.

While the country waits to experience the first effects of these sweeping healthcare reform changes, Sarah Moreland addresses potential shortfalls of the Mental Health Parity Act of 2008 with recommendations for new legislation to protect Americans with mental health conditions. On the scale of multinational efforts abroad, Piyali Kundu investigates the effectiveness of cigarette taxation policies in the European Union, highlighting where this public health effort might have led to the spread of smuggling, organized crime, and potentially increased consumption in some European markets. Finally, Allison Marron illuminates the hurdles met by polio inoculation efforts in Nigeria and Michael Cross analyzes the science behind the development of varicella vaccine schedules. From issues of governance in Nigeria on the front of the global polio eradication effort to fighting homelessness through preventing discrimination against individuals with mental health needs, this issue has something to appeal to a spectrum of public health interests.

In the realm of health science and improving practices through evidence-based medicine, *TuftScope* offers Lauren-Elizabeth Palmer's Feature Interview with Kevin Pho, MD, a web-savvy physician-blogger determined to improve primary care. Additionally, Max Leiserson examines the digital, wireless, and globalized future of medical imaging technology. From the scientific perspective, Alan Hsu explores genome-wide association studies aimed at identifying the etiology of diseases, while John Salvatore analyzes findings supporting the theory that oxytocin imbalance plays a central role in autism spectrum disorders. News and Views and Research Highlights both return in this issue to provide an overview of current medical news.

As the year comes to a close for *TuftScope*, the implementation of new ideas and the induction of another generation of *TuftScope* editors have proven the sweeping improvements set out in early 2009 a success. Due to the assiduous efforts of our online team, the new website has led to the establishment of the *TuftScope Blog*, whose constant updates provide a window into current healthcare developments. The accompanying online automated submission and review system provides a streamlined means for authors to find a venue to voice their views. Additionally, the hundreds of unique visitors to *TuftScopeJournal.org* each week have access to our older and newer material, all archived and available for download and further reading. We are pleased to announce that in recognition of these efforts, *TuftScope* was the recipient of the 2009-2010 Tufts University Office of Student Life Imagination and Innovation Award.

It was a pleasure serving the journal during this exciting time for *TuftScope*. This issue would not be possible if not for the coordinated efforts of the Editorial Staff. Special thanks are owed to Professor Harry Bernheim for his indispensable counsel, Lauren-Elizabeth Palmer for overseeing the transition, Max Leiserson for managing the online platform, Eliza Heath for her invaluable layout and design work, and lastly Alice Tin and the TCU Senate for financial guidance and support, respectively.

We hope you enjoy the issue!

Sincerely,

Michael Shusterman and Ron Zipkin

Health, Ethics, and Policy

Eriene-Heidi Sidhom, News and Analysis Editor

New Genomes Decoded Reveal Genetic Variations and Clues to Evolution

Eriene-Heidi Sidhom

The genomes of South Africa's Archbishop Desmond Tutu and an indigenous Bushman from Namibia have recently been decoded and the results were published in an issue of *Nature*. The goal of this study is to eventually enable researchers and drug companies to personalize medicine for people of all ethnicities and societies; until now, most of the genomes that were decoded were those of Europeans.

The publication of individual human genomes is controversial because of the risk of it being used against the individuals to deny them claims to property and leading to workplace and insurance discrimination. However, early analysis has revealed 1.3 million genetic variations not previously found and could lead to important insights. It also provided clues to human evolution. The researchers' interest is in this indigenous population in particular because they are believed to represent the oldest lineage of modern humans and are much more diverse than other populations. It is this genetic variation that might be used to explain their unique characteristics like their good sense of hearing, vision, smell and physical abilities.

Reference: Stein, Rob. (2010, February 18). Genomes of Archbishop Tutu, Bushman decoded in developing-world health push. *The Washington Post*.

The 10:23 Campaign: Homeopathy Skeptics Protest with Mass 'Overdose'

Ron Zipkin

At 10:23 AM on January 30, 2010, skeptics lined up in front of Boots pharmacies across Britain to participate in a mass 'overdose' of homeopathic remedies, emptying their pill bottles with the catchphrase, "There's nothing in it!" No protesters were reported harmed. This is the work of the 10:23 Campaign, sponsored by the Merseyside Skeptics Society, a new protest movement decrying the acceptance of homeopathy as an efficacious alternative medicine. Homeopaths claim to treat illness using the principle of treating 'like with like'; e.g., those experiencing symptoms which might be induced by arsenic oxide poisoning are advised to consume dilute solutions of the toxin.

The Campaign's use of the number 10²³ alludes to Avogadro's constant, and is intended to rebuke the dosage system of homeopathic remedies, which are often times so diluted they are unlikely to contain even a single molecule of the active compound. In fact, in homeopathic dosing 'higher potencies' are more dilute. In England, the National Health Service spends a reported £4 million a year on homeopathy. Though not as popular in the US, homeopathy is widely accepted in Europe

and elsewhere, defended by the Society of Homeopaths and other groups representing supporters of complementary and alternative medicine ("CAM").

Reference: 10:23: Homeopathy - There's Nothing In It!, <http://www.1023.org.uk/>



Arsenicum Album: a therapeutic dose of arsenic or sugar pills?

Image Richard_Craig(Flickr.com)

Possible Future Treatment for Chronic Fatigue Syndrome

Sangita Keshavan

In a college student's life, fatigue is a common complaint. But most college students would blame their exhaustion on a late night, or on having too much on their plate. Most, however, would not consider their case as extreme as that of Lynn Gilderdale, whose experience with chronic fatigue syndrome or myalgic encephalomyelitis (CFS/ME) left her in a paralyzed state.

Described as "progressive, paralyzing and commonly fatal," CFS/ME has devastating effects largely because of the depression associated with it. It is correlated with depression – the reason for the increased mortality in patients with CFS/ME is largely because of suicide. People with a history of depression are at increased risk for CFS/ME. The article cites the National Institute for Health and Clinical Excellence (NICE) as recommending cognitive behavioral therapy and graded exercise therapy for CFS/ME in adults and children. Children have been shown to have better outcomes. Patients with severe CFS/ME do not show considerable improvement despite such programs; however, if these programs are adapted, they can act as triggers for recovery.

There are dangers of a defeatist attitude amongst doctors. Doctors do not want to become entangled in such a sensitive and difficult issue. Because many are reluctant to accept CFS/ME as a real disease, some believe that we must stress the incurable aspects of the disease and the fatal possibility – something that could be damaging to patients. Alternative

treatments must be used, such as physiotherapy, community support and dietetic advice. Professionals should take into account the multitude of influences on people.

Reference: *BMJ*. 2010;340:c738

Do the Hazards of Sunbed Use Merit Legislation?

David Gennert

Recently, the use of indoor tanning booths has come under intense scrutiny from researchers and governmental groups, including an FDA advisory committee in late March that recommended that minors be banned from using the devices. The committee cited a “growing body of literature” suggesting a link between indoor tanning and skin cancer risk. The situation is especially worrisome in the UK, where a recent survey puts the prevalence of tanning bed use among those under 18 higher than the prevalence in the United States and other European countries.

A major problem is the misuse of tanning devices through the lack of compliance with regulations regarding device operating specifications and information given to consumers. An article in the *BMJ* cites studies in Europe that show the UV intensity for many tanning facilities was over the recommended limit, and 71% of sunbed facilities in Ireland did not know the type of UV light used. The article cites findings in Britain that described that many users of tanning facilities were not given information about potential harms, and substantial numbers have used tanning beds at home or in unsupervised facilities.

One possibility to help decrease this misuse of tanning facilities is to instigate a voluntary code of practice for operators of tanning facilities, but the article cites a study in Australia that described the number of facilities that disregarded regulations regarding age restrictions (more than half of facilities), skin type of users allowed to tan (90% of facilities ignored the code), and eye protection (14% gave inadequate or no eye protection).

With France and Scotland banning those under the age of 18 from access to artificial tanning and the EU passing regulations limiting the access of the same age group, it seems important to also include the enforcement of any regulations as a priority as well.

Reference: *BMJ*. 2010;340:c990

Massachusetts Leads the Nation in Flu Vaccines

Karen Chen

In a recently released state report, Massachusetts has been named the #1 state in the nation for vaccinating its residents against seasonal flu and H1N1. John Auerbach, commissioner of the Massachusetts Department of Public Health, says that the mobilization against swine flu in the state was a successful one. This success is evident by the fact that 36% of residents were vaccinated for swine flu, compared to the 21% nationally, about 2 million doses of the H1N1 vaccine were administered in Massachusetts. In addition, 57% of Massachusetts residents received seasonal flu vaccinations, as compared to the 37% national rate.

While H1N1 was declared a pandemic, it did not cause nearly the number of deaths that were feared. In Massachusetts, 32 deaths were confirmed due to swine flu, and all except 5 of the cases involved underlying medical conditions. The state was prepared with years of pandemic planning, and local health departments, school systems, and hospitals sent out public health messages through brochures, online forums, *Twitter* feeds, and 30-second videos in movie theaters. Auerbach says that “the chances of coming down with H1N1 are diminishing in Massachusetts.” A third of the population already had H1N1, and another third has been vaccinated. Public health specialists hope this will provide “herd immunity,” as there are not enough people sick with or susceptible to H1N1 for it to easily spread.

Reference: Cooney, Elizabeth. (2010, March 21). Mass. tops nation in flu shots, report says. Boston.com.

Chronic Disease in Children

Eriene-Heidi Sidhom

Three groups of children, spanning from 1988 to 2006 included in the National Longitudinal Survey of Youth (NLSY), were analyzed. The study revealed that chronic conditions more than doubled. One explanation could be that better access to care might have resulted in the increased diagnosis of chronic conditions. For example, the survival rates for cancer, prematurity and congenital disorders have increased beyond which was imaginable a little while ago. Additionally, in 1998 the federal Maternal and Child Health Bureau expanded the definition of children with special health needs to incorporate physical, developmental, emotional and behavioral conditions.

Furthermore, there seemed to be evidence of dynamic changes in onset, duration and resolution of these chronic conditions. In order to determine whether these changes were real, NLSY identified chronic conditions through questioning the parents on the condition of the child. The findings of the surveys supported these dynamic changes and from a developmental perspective, these dynamic changes are to be expected in childhood. For example, asthma can be influenced by the onset of puberty, stressful transitions or changes in family environments.

The increase in chronic conditions seemed to be driven by an increase in obesity, a slight increase in asthma, but little change in learning and behavioral problems, despite increases in ADHD and mental disorders. These findings raise the question of whether there is a link between asthma, obesity and ADHD. In fact, there is evidence that high levels of early childhood stress may result in poor executive function and impulse control. As can be seen, obesity is not the only childhood condition that needs to be dealt with, and prevention of childhood diseases also prevents age related diseases as adults. Therefore, the need for change, as well as the results of inaction, is too big to be ignored.

Reference: *JAMA*. 2010;303(7):665-666

Eliminating Transfats from Food

Benjamin Scoblionko

As America's economic problems continue to grow, so too do our waistlines. In 2009, almost two thirds of United States residents were overweight or obese.² As families look for inexpensive alternatives to weather tough times, they turn to fast food and cheap candy bars for dinner and snacks to fill the void in their stomachs and bank accounts. Many of these fast food chains, candy and cookie companies, such as Wendy's®, Lays®, and Kraft®, have started following the growing desire of Americans to line our grocery store shelves with healthier options by eliminating transfats in many of their products.⁴ Transfats are fatty acids that undergo industrial processing that adds hydrogen to liquid vegetable oils.⁶ This process, known as hydrogenation, increases saturation, melting point and shelf life, which makes these oils very attractive products to cook with.

The problem with this is that, unlike natural fats, transfats are not essential; they lower HDL cholesterol levels and increase the risk of heart disease. One would think that because of the reasons previously stated, the use of transfat containing oils would be banned, but that is not the case. The National Academy of Sciences (NAS), the association that advises both the United States and Canadian governments, concluded that there is "no adequate level, recommended daily amount or tolerable upper limit for trans fats. This is because any incremental increase in transfat intake increases the risk of coronary heart disease."⁵ In spite of this conclusion, the NAS has yet to recommend the elimination of transfats from daily diets.

Transfats are very popular and are widely used because their impact on melting point and shelf life. These small benefits come at a huge cost for the American population. Last year, obesity-related diseases cost an estimated \$147 billion.² Obesity rates did not decrease in a single state in the US in 2009.³ These staggering statistics show the impact unhealthy food, and specifically transfats, is having on our hearts and checkbooks. One way to reduce this problem would be banning the use of unnaturally occurring transfats (some transfats, known as vaccenic acids, naturally occur in trace amounts in meat, but do not have the same negative effects). The current laws allow food corporations to advertise products that contain less than half a gram of transfats as having zero grams of transfats. This is not transfat free and is only misleading Americans. Although many of the major food production companies are leading by example by switching to trans-fat free oils, there is still much progress to be made.

Organizations, such as "Bantransfats.com," have led the charge facilitating the elimination of transfats by bringing the problem into mainstream media. Following the Bantransfat.com vs. Kraft® law suit in 2003, Kraft eliminated trans fats from over six hundred products, including Oreos®.¹ In addition, as a result of the law suit, the FDA labeling rule was passed, requiring transfats to be listed on all food labels. Although cases such

as this one have helped to initiate awareness of the dangers of transfats, the problem continues largely to be ignored by the government. The only way to eliminate the negative effects of transfat is to completely eliminate the use of unnaturally occurring transfats.

Walter Willet, from the Harvard School of Public Health, has been pushing for the much needed reform. Willet spoke to a group of food manufacturing companies and professions advocating that, "Human life is more important than shelf life."⁷ The movement towards a transfat-free America Willet desires has been a slow process because of the simple fact that most Americans do not understand what transfats are and how they affect the body. An important step that has helped publicize the nutritional distinctions among different types of fats came with the well-advertised New York City restaurant ban.⁷ This was an important step in the right direction, influencing legislation in other major cities, such as Boston where transfats were banned in 2008.

As cities such as Boston and New York City lead the way, the understanding about the toxic effects of transfats continues to grow. In recent years, strides have been made in the right direction, but there is still room for improvement. Health curriculums must continue to follow the example set by New York City and emphasize the importance of healthy eating and the elimination of transfats. The obesity problem in America has turned into an epidemic that, in recent years, has spiraled out of control. A national ban on transfats would not only start the much needed transition to a healthier America, but should help reduce obesity costs.

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Multivitamins in Medical Treatment

Lori Fingerhut

Vitamins have been the face of wonder drugs since the late 1980s. It was thought that taking a daily extra dose of vitamins would protect against cancer, heart disease, kidney disease, diabetes, and several other diseases or disorders. Recent studies, however, have not only indicated that vitamins may be less effective in treating these maladies than originally thought, but have also found that taking a daily vitamin could be detrimental to one's health. Has the hype of supplemental vitamins officially died?

It was approximately forty years ago that biochemist Linus Pauling suggested the use of "megadose" vitamins, or orthomolecular therapy as it was termed, for the prevention and treatment of cancer. Ten years later, daily use of vitamin supplements became the new craze.¹ These days, multivitamins are the most common dietary supplement taken in the United States, and many studies are done on the effectiveness of multivitamins and other individual supplements.² There is little argument for the nutritional value of vitamins. In a study published by the American Journal of Clinical Nutrition, the nutrient adequacy of 17 nutrients for those who take a daily multivitamin was shown to be 8 percentage points higher than those who did not take the daily supplement.² Additionally, physician and nutritionist Walter Willett, chair of the Department of Nutrition at the Harvard School of Public Health recommends taking a multivitamin because "there are a few nutrients that are marginal in many people's diets, even if they are very health conscious."³ Some of these nutrients include folic acid, vitamins B6 and B12, and vitamin D.

It seems that individuals who take supplements are already receiving much of their vitamins from the foods they eat. Therefore, taking multivitamins can cause the excess intake of several particular vitamins, such as vitamin A, iron, and zinc.² There has been much speculation about whether this excess is as effective for reducing the risk of certain diseases as was originally thought. Dr. Harvey Simon, a physician and professor at Harvard Medical School and founder of Harvard Men's Health Watch, has abandoned the notion that vitamins could help prevent chronic illnesses like cancer and heart disease. According to Simon, not only do vitamins not prevent diseases, but they can actually cause more harm.⁴ A study by the University of Washington on the effect of vitamin E on lung cancer, for example, found that the relationship between increased vitamin E supplements and lung cancer was statistically significant. Another study, published in the Journal of the American Medical Association, found that in 47 randomized trials of antioxidant supplements, the use of vitamin E, vitamin A, and beta carotene increased the rate of mortality by 5 percent.¹

Many in the scientific community support conclusions like Dr. Simon's. Pamela Mason, a London Health Service Information spokesperson explains, "(Vitamins) were never

intended to be used to prevent chronic disease such as cancer."⁵ Additionally, the U.S. Department of Health & Human Services Agency for Healthcare Research and Quality issued a statement in 2003, published in the Annals of Internal Medicine, indicating that there was not enough scientific evidence to prove a connection between vitamin use and lower risk of cancer and heart disease.⁶

Physicians, nutritionists, and other experts do not deny the benefit of vitamins on health. As Marian L. Neuhouser, member of the Cancer Prevention Center at the Fred Hutchinson Cancer Research Center in Seattle, said, "we call them essential nutrients because they are."¹ What the experts stress, however, is the maintenance of adequate nutrition through a balanced diet; one that will provide you with the necessary vitamins in appropriate concentrations. Even Walter Willett, advocate of the use of multivitamins, says on the topic of taking multivitamins, "It's a safety net that can fill nutrient gaps. It's not a replacement for a healthy diet."⁷ The best solution, at least for those who are able to maintain a balanced, healthy diet that is already full of nutrients and vitamins, would probably be to nix the multivitamins and replace it with only those supplements whose daily recommended values are not met by the average diet.

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Lori Fingerhut is an Assistant Editor for TuftScope.

100 Years after Flexner: Reconsidering Premedical Education

Michael Shusterman

In the early twentieth century the proliferation of for-profit medical schools and unstandardized curricula led to calls for drastic change. Medical schools operated under widely disparate models ranging from apprenticeship systems to university-based lectures. Physicians practiced with inadequate levels of training in both clinical and scientific medicine. Whereas previous efforts at reform by the American Medical Association (AMA) had proven ineffective during the 19th century, the advent of scientific medicine shifted the balance of professional opinion.¹ To reevaluate medical education in the United States, the AMA created in 1904 the Council on Medical Education (CME), tasked with standardizing admissions requirements to medical school and reforming medical school curricula and preclinical training.² In 1908 the CME and the Carnegie Foundation commissioned a report on medical education in the United States, led by education theorist Abraham Flexner, PhD.

Flexner undertook a rigorous survey of the 155 medical schools operating at the time and submitted his suggestions for reform in 1910 as the *Report on Medical Education in the United States and Canada*, more commonly referred to as the Flexner Report.³ The Flexner Report's recommendations for medical education and admissions would serve as the foundation of the medical education system in the United States. Flexner strongly believed in the combination of scientific education with clinical practice, a consequence of following the university-based medical systems of Germany and France at the time. The resulting standardization of medical education was the 2+2 model of two years of science followed by two years of clinical practice. Today this curricular model is being challenged by a movement focused on shifting medical education towards a future when personalized genomic medicine may become available.⁴ Similarly, science requirements are being condensed from 2 to 1.5 or fewer years in the hope of exposing medical students to clinical practice more rapidly.

However, whereas graduate level medical education has continued to evolve since the introduction of the seminal Flexner Report, the same has not been the case for premedical education requirements. Flexner advocated for a rigorous model of medical education based upon the laboratory scientific tradition. This led by the 1930s to the current set of standard requirements for admittance to medical schools—1 year of biology, 2 years of chemistry (general and organic), and 1 year of physics.⁵ Since then a vigorous debate has continued on the importance and necessity of various subjects for medical school preparation.⁶ Some have called for a rigorous reconsideration of the entire scope of medical and premedical education.⁷ Emmanuel has argued that “many premedical requirements are irrelevant to future medical education and practice.”⁸ He has proposed exchanging the traditional organic

chemistry, physics, and calculus requirements for courses on genetics, molecular biology, biochemistry, and statistics. Emmanuel argues that these new courses should be integrated with a strong background in the social and ethical dimensions of healthcare (policy, bioethics, social sciences).⁸ In a recent assessment of science requirements for both medical school education and baccalaureate level preparation, Lambert and colleagues agreed with Emmanuel's assessments in exchanging the physical sciences for coursework devoted to biomedical and molecular principles.⁹

Others have looked towards Lewis Thomas' more radical suggestion of eliminating the majority of standard scientific preparatory requirements in favor of a broad liberal arts education.^{10,11} Thomas argued that the loss of the liberal arts education had degraded the humanistic integrity and ethics of rising physicians who were willing to sacrifice professional and scientific values in an endless race to the top. Analyses have overridden fears that humanities majors are incapable of performing adequately in medical school. In a review Wershof et al. have shown that medical students who majored in the humanities and only took the minimal premedical requirements perform on par with students with more extensive preparation in the sciences.¹² However, this push for the integration of humanities into the curriculum has met with an opposing effort to spend more time on the sciences. A recent colloquium on evolution and medicine came to the conclusion that physicians require far greater exposure to evolutionary biology and that the subject should be incorporated throughout the medical education system.¹³

What then are we to make of these disparate opinions? One potential solution may lie in the proposals of a joint Association of American Medical Colleges (AAMC)-Howard Hughes Medical Institute (HHMI) report, *Scientific Foundations for Future Physician*.¹⁴ The AAMC-HHMI study urges the adoption of the scientific competencies for medical and premedical education, with a focus on integrating core focus areas into interdisciplinary courses rather than rigid medical requirements. For instance, organic chemistry and biochemistry may be combined into a year long sequence that incorporates organic chemistry topics into the broader scale of biochemical principles. Similarly courses in the physical sciences may utilize systems such as neural networks to study electrical systems and consider Newtonian principles in the context of biomechanical systems. The report recognizes the difficulty in implementing such interdisciplinary courses across traditionally compartmentalized science departments in universities. Additional problems may ensue from resistance among faculty, particularly in the physical sciences, to incorporate greater

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emphasis on biological topics in coursework. However, since 2006, Harvard University has been successful in implementing a framework that has integrated biomedically relevant topics into typical premedical coursework.¹⁵

It would seem prudent for universities to reconsider the current design of premedical coursework in light of the changing attitudes among medical educators and students. Significant progress has already been made in the area of introductory biology reform through the inclusion of genetics, molecular biology, and physiology into preliminary biology courses. Further steps must result in the creation of an integrated organic chemistry and biochemistry sequence. Rather than eliminating organic chemistry this will reinvigorate the subject by forging a union between basic science and biochemical systems relevant to medical study. Finally, coursework in introductory physics should seek to incorporate biological principles, where possible, into curricula. Once implemented these initial reforms should serve as a catalyst for additional reconsiderations and changes to premedical requirements. It seems appropriate that 100 years after the Flexner Report serious efforts should be taken to once again reevaluate the paradigm of medical preparatory education.

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RESEARCH HIGHLIGHT

Larger Hospitals Associated with Lower Mortality for Three Common Conditions

Caroline Melhado

A recent study published in the *New England Journal of Medicine* found that patients suffering from acute myocardial infarction, heart failure, and pneumonia had lower rates of death after 30 days if they were admitted to a larger hospital. A review of standard Medicare analytic files demonstrated that patients admitted to a larger hospital had a reduction in mortality, however this reduction hit a threshold level, as reduction was insignificant as the hospital volume grew past the threshold.

The study included 734,972 patients of myocardial infarctions from 4,128 hospitals, 1,324,287 patients with heart failure at 4,679 hospitals, and 1,418,252 patients admitted with pneumonia at 4,673 hospitals. Hospitals not included were those that had fewer than ten patients annually. Researchers found that increasing the annual volume by 100 patients in a hospital was correlated to a 20% reduction in death after 30 days for patients admitted with acute myocardial infarction. Likewise heart failure showed an increase by 100 patients annually would lead to a 10% decrease in 30-day mortality, and a 5% reduction of mortality for patients with pneumonia. However, when the volume of a hospital reached 610 patients, the decrease in 30-day mortality was no longer significant for myocardial infarction. Thresholds for heart failure and pneumonia were 500 and 210, respectively.

Of the hospitals included in the study 25% were teaching hospitals, and 27% had cardiovascular revascularization services. While larger hospitals were more likely to have these characteristics, stratification of each of these components showed that they were not significant confounding variables. Limitations to this study are that only these three conditions were studied, and therefore the widespread application of larger hospitals for many more common medical problems might not follow this trend.

As policy makers grapple with ways to improve the healthcare system, researchers are studying ways to improve the outcomes of patients with common medical problems. While both negative and positive outcomes of these three conditions at large and small hospitals existed, the overall reduction in mortality at larger hospitals might shape future public health policy to favor larger medical institutions.

Reference: *NEJM* Volume 362:1110-1118

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FEATURE INTERVIEW

A Conversation with Kevin Pho, MD

Lauren-Elizabeth Palmer

Kevin Pho, MD, is a practicing primary care physician in Nashua, New Hampshire, as well as creator and author of KevinMD.com, a leading blog for healthcare commentary. KevinMD.com provides a rare physician's perspective on current and provocative views in healthcare today. It was voted the best medical blog of 2008 and has appeared on top blog lists on Forbes.com and CNN.com. Dr. Pho has been cited in "The Wall Street Journal", "The New York Times", "British Medical Journal" and "Newsweek" to name a few. He has also appeared on the CBS Evening News with Katie Couric and is a member of "USA Today's" Board of Contributors.

Why did you decide to begin your medical blog?

Well, I first began blogging because I noticed there was really so little information available to the public as to what a physician's opinion might be on current medical news. I was really surprised at how it took off and offered me so many opportunities to share my opinion with colleagues and patients and to the general public. I wanted to fill this void, the seeming lack of a physician's voice.

You've mentioned that other members of your practice read your blog. How does having a blog change the social or professional aspects of being a doctor?

My partners and all of my colleagues locally and even patients are aware of what I do, so professionally it has given me a lot of opportunities that I don't think I would have had - opportunities to write for large publications like *The New York Times* and *USAToday*, for instance. It has given me a connection with patients and made my patients more aware as they are able to find me on the internet by doing a Google search for me. I'm known as a doctor who is relatively technologically savvy and that appeals to a certain demographic.

What role do you envision the internet playing for the next generation of doctors?

I think the internet is going to be closely intertwined with what we do and I think it will be to every doctor's benefit to have some internet presence. A growing number of patients are finding health care information online and it's not only health information, they are researching their doctors and hospitals. From a marketing standpoint, it's very important to be online. You want to have control over your name online - for instance you don't want people to find your name and see a negative news article. For the current generation of medical students, things like Facebook are more second nature, so they will have an easy time embracing the internet as part of their practice. It's the older generation that will have a harder time embracing these technologies.

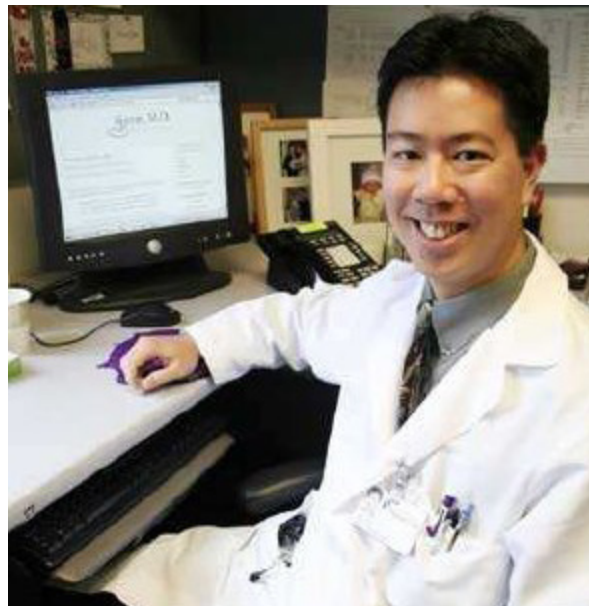


Image from www.KevinMD.com

What potential does social media hold for doctor to doctor communication?

I think there is a lot of opportunity. There are doctors on *Twitter*. You'll see doctors who go to conferences and tweet updates. When a study is breaking they communicate via *Twitter* and get instant analysis and instant opinions on what is going on in breaking medical news. Part of the power of social media is the immediacy of the medium; these things can be discussed just as news is breaking. Previously you would have to wait for an article to be published in medical journals whereas now things can be discussed right as the news breaks. So yes, I think things like *Facebook* and *Twitter* offer a tremendous opportunity for doctors to collaborate with one another. You are seeing medical journals already on *Facebook*, *The New England Journal of Medicine* is on *Facebook*. You are seeing medical societies already on *Twitter* like The American Medical Association and The American College of Physician, and I think that will be a growing trend as the medium is so powerful and so attuned to collaboration.

There seems to be some resistance among physicians to technology. As someone who obviously reaps a tremendous benefit from technology, why do you think this resistance is there?

I'm not sure there is resistance to the actual technology. I think with the way our health system is structured, there is no incentive for doctors to embrace technology. Not a lot of health insurers pay doctors to spend the time to email and get on social networks so I don't think there is resistance to it but I think the health system needs to provide incentives to get on these technologies. Doctors are busy enough. I am a primary care doctor and I and a lot of my colleagues see like 25 to 30 patients a day and you add on top of that social media and emailing patients, which is not reimbursed, and that doesn't provide doctors with a lot of incentive. Health insurers should give that push as it provides doctors with a

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way to communicate with patients and patients themselves can benefit from the easy access they would have to medical professionals.

As an internist how do you find the time to maintain your blog and interact so much with social media?

It's certainly a time commitment, and obviously I'm on one end of the spectrum. There is a tremendous benefit to participating in social media, but I also spend a lot of time on it. Personally, I do it after my family goes to sleep. I'm going to be honest and say it does take a certain time commitment, but I wouldn't do it if I didn't get a tremendous reward out of it.

As a primary care provider yourself you have particular insight as to the nation's current crisis of internists. Given your expertise, how do you think we should address our shortage of primary care physicians?

That is a common issue on my blog and I think any foundation of health care reform needs to have a strong base of primary care. It comes down to two things: first, there is the disparity between salaries of primary care physicians and specialists. Currently most specialties have much higher salaries than primary care has. Second, there is the lifestyle difference. Primary care is inundated with a lot of bureaucracy that really interferes with the doctor patient relationship and when you take those together there is really not a lot of incentive for medical students and future doctors to go into primary care. The solution is twofold: we need to improve the practice environment and the lifestyle of the primary care doctor, remove the bureaucracy and any obstacle that impedes the doctor-patient relationship, and secondly we need to improve the disparity between what primary care doctors and specialists make. If you are a medical student, and the average student has \$130,000 worth of loans when they graduate, you are going to see these issues and the choice for many is pretty clear. *The Journal of the American Medical Association* found a couple of years ago that only two percent of medical students plan to go into primary care/ internal medicine. Take that number and extrapolate it to the future. We're talking about things like universal health care and we need more primary care doctors so I think the shortage will become starker as we move forward.

You mentioned universal health care. As a physician, what is your perspective on the current bill for health care reform?

I think the bottom line is that the status quo is not acceptable. Currently we have close to 50 million Americans who are uninsured and health care costs account for almost 20% of gross domestic product. If nothing is done then those problems will worsen as time goes on and will really bring the American economy to its knees. So something needs to be done; the question is 'how to do it'. I'm going to stay apolitical, but we need to find a way to cover more Americans and control health care costs, but underlying that would be increasing the number of primary care doctors. If we cover everybody, and we have more patients, then we need more primary care doctors. There is going to be more pressure in the future to look for primary care doctors and, I've said this before, what is the point of having insurance if you can't find a primary care

doctor to see you? The bottom line is we need to find more doctors to take care of people and that is definitely a bipartisan problem.

You've mentioned a few times the problem of soaring health care costs so , on this topic, what do you think is the biggest culprit in terms of wasteful medical spending?

There is a lot of medical waste that goes on. Many doctors don't have electronic medical records and often because of that tests get duplicated. Also the way a lot of doctors are compensated is a problem as most doctors are compensated on a fee for service basis and that encourages more doctors to prescribe more tests because that is, frankly, how most doctors get paid. Research at Dartmouth has found that, because of this financial incentive, there is a wide disparity in our country as to how much doctors spend. I think secondly we have this problem of so called defensive medicine which is practiced to avoid the threat of malpractice lawsuit. Currently our malpractice system is very uneven as to how it punishes doctors and compensates patients and because of how uneven and unpredictable the system is doctors have another incentive to order more tests to prevent the threat of a malpractice lawsuit. I could certainly go on but if you were to name two of the biggest culprits it would be the way doctors are compensated and the way they to practice to avoid a lawsuit.

How do you avoid the trap of defensive medicine in your own practice?

The best way is to communicate with patients. You always have to be more open and discuss all of the options. Multiple studies have shown that doctors who have better relationships with patients and who have open lines of communication get sued less. The problem is we operate in a system where time with patients is not valued. Doctors are always encouraged to see as many patients as they can and there is really a conveyor belt mentality as to the way the system encourages doctors to practice. So the best way to reduce malpractice lawsuits would be to first off explain every medical decision you make and explain the risks and benefits and come up with shared decisions. And secondly, if a mistake is made, open the lines of communication with the patient, apologize to them, and explain what happened. Studies have shown that doctors who offer a sincere apology to patients get sued less.

There is currently a move in health care toward digital medical records to which there seems to be some resistance among physicians. Why do you think this is?

I think the idea of digital medical records is good and the ideal would be for the entire country to be running on the same digital medical record system, similar to what the Veterans Administration uses for their system. The problem with Digital medical records right now is there are so many competing systems and they all can't talk to one another. If I had a patient who was admitted to the hospital now under their system and then that patient saw me for follow-up and I use a different system there is no way for my electronic system to communicate with the hospital's system so it's very fragmented and the fact that they can't talk to each other is a big problem. If I had my ideal,

a very simple idea would to have all of the systems equipped to communicate with each other so tests aren't repeated. The other thing is a lot of the interfaces aren't up to standard. If you look at Google and Facebook the interfaces that they use are very intuitive and easy to use. A lot of interfaces of the current generation of digital records are somewhat archaic and make it difficult for the doctors. Doctors are already pressed for time so if you encourage them to use a tool which doesn't improve their lifestyle or practice environment there will be obvious resistance. I think the first thing these digital medical records have to do is prove themselves as tools that make doctor's lives easier, and right now that is not the case.

What role do you think Comparative Effectiveness Research should play in a physician's practice and do you think a physician will accept redefined principals?

It's a good idea. I do believe that doctors should practice based on the best available evidence. If you look at some studies based on Medicare spending, different parts of the country spend a different amount of healthcare dollars because of the variation of care nationwide. If you look at a heart attack patient in Miami, FL the cost and amount of medicine that patient will receive is different from say Minneapolis, MN. So if you had doctors practice according to the same evidence based set of guidelines that will help out in the variation. The problems you have are because comparative effectiveness reduces medicine down to so called cook-book medicine and doesn't take into account the individual component of a single patient. It really depersonalizes medicine and that is one of the problems. If you base comparative effectiveness on studies that cannot encompass every patient you encounter. So I think it's good, but there needs to be flexibility for individual cases. If you could address those concerns, you are going to find more doctors accept comparative effectiveness, because that is the problem: it doesn't allow for individual treatment decisions that may occur outside the set of guidelines.

What do you think of the recent proposed guidelines in mammography and the media backlash?

You are referring to the task force recommendation that doctors discuss whether a mammogram would be suitable for women ages 40 to 50. Of course there is a lot of controversy on that so I think the problem is communicating with the public. There is a pervading belief among the public that more testing is better and that goes for cancer screening. People think that if you get a mammogram early and get them every year that naturally leads to better care, and that's not necessarily the case. There is a downside to cancer screening. There are a lot of benign diseases that can get detected, which sometimes leads to a further invasive test like a biopsy. I think communicating the idea that more cancer screening isn't necessarily better is a difficult idea to communicate. I think the task force just publicized their recommendations without any surrounding nuances and so I think they were partially responsible for the controversy. In terms of what I think, it has to be a shared decision between the doctor and patient. When I have a healthy woman in my practice who is 40, I discuss cancer screening. I certainly discuss the risks and benefits of mammogram and

we come to a decision between myself and my patient. The decision could be to go ahead and do a mammogram and it could be to not. I think, bottom line, it has to be a decision between the doctor and patient and it is up to the doctor to really explain the risks and benefits of going ahead and doing a mammogram.

What experience have you had in your 6 years of almost continuous blog activity that really stands out?

I didn't expect it to be as big as it is and I am certainly gratified that people are as interested as they are. It's certainly given me opportunities that I wouldn't have had otherwise, opportunities like writing for publication such as *The New York Times*, being a regular columnist for *USAToday*, appearing on *The CBS Evening News* and being invited to speak and talking to you for instance, I think it's really been enlightening and I think it has forced me to think about issues on a deeper level. In all social media you get continuous feedback, you get posts to the blog, you get conversation on twitter so whenever I write something I get instantaneous feedback on what I think. This has allowed me to see other views and whether they agree with me or not, it's allowed me to really think deeper on a lot of issues.

Do you think that having this connection via social media has made you a better physician?

Absolutely. When I talk to patients, even on a superficial level, it makes a difference. When patients come in with an article they've read earlier that day chances are I've already read it just because of the sheer amount of reading I do. And secondly on controversial issues like mammograms or drug recall, I'm able to get an instant opinion of a variety of medical viewpoints so it's really beneficial to me. When patients come to me with these issues I'm able to present to them a more informed opinion.

What advice would you have for other health care professionals who are interested in sharing information in the way that you have done?

I think first off I would say 'go for it'. I feel very strongly that medical professionals need to be online, not only to help their practice out, but also because patients need guidance as to what medical information is reputable online and it's really our responsibility to get online and be that source of reputable medical information. That said, there are certain pitfalls that I want everyone to avoid: first off, patient privacy has to remain paramount. It's very easy on *Twitter* and *Facebook*, for instance, to accidentally disclose patient information, and with the strict privacy rules of HIPPA any medical professional needs to be cognitive off that. Secondly, I wouldn't give any medical advice online. [Internet cases] are still relatively new, especially in terms of the malpractice field and so I wouldn't give any personal medical information online. But if you keep those two things in mind, there shouldn't be any reason why any medical professional shouldn't embrace the internet. I think it can help not only their practice but also their patients as well.

Summaries of Medical Research of Interest

Caroline Melhado, *Research Highlights Editor*

Only Severely Depressed Affected by Anti-Depressants

A recent study found that common anti-depressants only helped the severely depressed, while people with milder forms of depression on the anti-depressants exhibited little to no difference compared to those on a placebo regimen.

The meta-analysis included six studies, which included 434 patients given anti-depressant regimen and 284 on a placebo regimen. The patients were rated on the Hamilton depression rating scale, with the lowest score among the trials being 10 and the highest a 39. Three studies used paroxetine, a serotonin reuptake inhibitor, and the remaining used imipramine, a tricyclic antidepressant. The study suggests that other popular, similar anti-depressants, such as Lexipro and Prozac, would show similar results. This analysis concerned patients older than 18 and did not perform a placebo washout period.

The studies all concluded that the presentation of true drug effects was a function of the severity of depression. Patients with a score of 25 or lower (mild to moderate depression) showed no difference between the placebo and anti-depressant groups. Conversely, those with a score of 25 or higher (severe depression) responded to the anti-depressant medication with increasing efficacy as their HDRS number increased.

Reference: *JAMA*. 2010;303(1):47-53.

Catheter Ablation as a First Line Arrhythmia Defense

A recent study found atrial fibrillation, a heart rhythm disorder, could be controlled by a procedure called catheter ablation more effectively than traditional antiarrhythmic drug therapy (ADT). Catheter ablation is a process that cauterizes muscles surrounding the pulmonary veins in an effort to destroy the tissue causing the abnormal electrical pulses.

The trial was conducted at 19 hospitals and included 167 patients that had had at least 3 atrial fibrillation episodes during the last six months. 106 patients were randomly given the procedure, while 61 were given a new form of ADT. Researchers found that 66% of catheter ablation patients were free of episodes nine months later, while only 16% of the ADT patients were episode free.

Five patients out of the catheter ablation group suffered from major treatment-related negative effects (4.9% of the catheter ablation group). Five patients from the ADT group suffered from ADT-related adverse effects (8.8% of ADT group).

Traditional ADT has re-occurrences on average of 50%, so catheter ablation is likely to be seen as an alternative first line defense against many cases of atrial fibrillation. Biosense Webster, the company that produces the catheters used in the procedure, funded the study.

Reference: *JAMA*. 2010;303(4):333-340.

Reduced Salt Intake Could Lead to Decreases in Medical Costs and Heart Disease

The New England Journal of Medicine published a study stating a decrease in 3g of salt per day for every individual in the US could lead to a drastic decrease in the prevalence of Coronary Heart Disease (CHD), stroke, myocardial infarction and death from these causes.

The study used a computer model, CHD Policy Model, to study the prevalence and mortality of CHD of a variety of ages and demographics within the US. Using the data from multiple studies correlating the effect of salt on systolic blood pressure, researchers were able to compare the impact of salt intake to a variety of health effects. They determined that a reduction in salt intake by 3 grams daily was a more effective way to prevent CHD, stroke and myocardial infarction than would a 50% reduction in smoking, a 5% decrease in body mass index and some treatments of

hypertension. The study showed that a decrease in salt intake would affect both white and non-white men and women.

A salt intake reduction of 3 grams would save an estimated \$10 billion and \$24 billion in yearly healthcare costs and would reduce the number of new cases of CHD by 60,000 to 120,000, stroke by 32,000 to 66,000, and myocardial infarction by 54,000 to 99,000 annually. Deaths from these three sources would be reduced by 44,000 to 92,000 a year. Researchers suggest that the cost-effectiveness of a state wide initiative to lower salt intake would save money in comparison to the medical costs that the US's salt dense culture creates.

Reference: *NEJM*. January 20, 2010 (10.1056/NEJMoa0907355)

Morphine May Lower Risk of Developing PTSD

A new research study found that the use of morphine directly following a traumatic experience significantly lowers the chances of developing Post Traumatic Stress Disorder (PTSD). The study examined soldiers who were admitted to navy-marine corps care during operation Iraqi Freedom.

Researchers examined 696 patients from the Navy-Marine Corps Combat Trauma Registry Expeditionary Medical Encounter Database. Soldiers who suffered traumatic brain injuries or lacked complete records were excluded from the study. Of the 243 participants who developed PTSD, only 61 were administered morphine. Of the 453 patients who did not develop PTSD, 76% received morphine. Even taking into account other variables such as age, injury severity, and amputation status, the correlation remained significant.

This research shadows a previous study that linked the use of morphine and other opiates to reduce the chance of developing PTSD in pediatric burn victims.

Researchers suggest that pharmacotherapeutic intervention may be a

method of second line of defense against PTSD not only in soldiers but rape victims, burn victims and others. While this was an observational study, and therefore causal inferences cannot be made, many doctors believe that opiates would block memory consolidation and subsequent fear responses after a traumatic event. Researchers were unable to fully develop a dose-response relationship because of the nature of the research.

Reference: *NEJM*. 2010; 362:110-117.

Most Effective HIV and TB Treatment

A study found that individuals who underwent combined-integrated therapy for both Tuberculosis and HIV survived remarkably better than individuals who received sequential therapy. Concomitant therapy is encouraged by the World Health Organizations, however many clinicians worry about drug interactions and the pragmatics of taking so many pills for patients. This randomized study was designed to find the most opportune time for patients with both TB and HIV to start antiretroviral therapy.

The study was conducted in Durban, South Africa and included 642 patients that had a positive diagnosis of tuberculosis and an HIV infection with a CD4+ cell count < 500 per ml³. The combined-integrated therapy group included 429 patients which received a standard tuberculosis treatment, prophylaxis with trimethoprim-sulfamethoxazole, and a once daily antiretroviral treatment of didanosine, lamivudine, and efavirenz. The sequential therapy group was designed to first be treated for Tuberculosis, using the same TB treatment plan, and start antiretroviral therapy upon completion of the TB regimen.

Researchers found that in the combined-integrated therapy group, the incidence of death was 5.4 for every 100 person-years of observation. The sequential therapy group saw an incidence of death of 12.1 for every 100 person-years of observation. After adjustment for various confounding factors, researchers found that patients in the combined-integrated therapy group had a relative risk reduction of 54%. Two and a half years into the study, the data and safety monitoring committee

recommended all patients be put onto the combined-integrated therapy regimen for the remainder of the study. The combined-integrated therapy group saw nearly three times the cases of immune reconstitution inflammatory syndrome. However, there were no deaths resulting from this syndrome.

Researchers concluded that antiretroviral therapy should be started during TB therapy to improve rates of survival in individuals with both an active diagnosis of TB and HIV. Even after controlling for complications resulting from drug interactions and regimen compliance, the risk ratio remains lower for combined-integrated therapy. This evidence further supports WHO's recommendation.

Reference: *NEJM* Volume 362:697-706

Serotonin and Tryptophan Hydroxylase Deficiency Found in SIDS Infants

A Harvard based research group found that victims of Sudden Infant Death Syndrome (SIDS) are most likely to have a decreased level of serotonin and its biosynthetic enzyme TPH2, tryptophan hydroxylase, when compared to control children. These lower levels would normally lead to a diagnosis of medullary 5-HT (serotonin) deficiency disorder, if caught before death.

Previous hypothesis of SIDS speculated that death was due to the inability of a baby to self-arouse after a life threatening event, such as asphyxia. The study aimed to find whether the inability to return to homeostasis was due to an elevated or decreased serotonin production. The study included post-mortem evaluations of serotonin and tissue from 41 infants. Seven infants, who had died from known causes other than SIDS were used as controls, as well as five infants who were hospitalized with chronic hypoxia-ischemia.

Researchers found that serotonin levels were 26% lower in babies who had died of SIDS. Tissue collection from the raphé obscurus showed levels of TPH2 were 22% lower in SIDS cases than in controls. The ratio between serotonin and TPH2 was consistent throughout both the SIDS cases and control cases.

From these results researchers extrapolated that SIDS death most likely due

to the insufficient amount of serotonin, due to the decreased levels of TPH2, to self-arouse during asphyxia. Authors of the study hypothesize that the low levels of TPH2 result from some unknown developmental reason, probably in the first or second trimester, that leads to the production of immature serotonin receptor binding sites and decreased levels of serotonin. Further animal testing might divulge how decreased levels of TPH2 arise during embryonic development and how this deficiency leads to sudden death during sleep.

Reference: *JAMA*. 2010;303(5):430-437.

Vitamins Ineffective in Lowering Pregnancy Related Hypertension

The New England Journal of Medicine published a study investigating the effect of supplemental vitamins in pregnant women who were at risk of hypertension. Researchers performed a double-blind, randomized test to test the efficacy of supplemental vitamin C and E in preventing pregnancy-associated hypertension. They found that the supplements did not significantly decrease the risk of hypertension or negative perinatal/maternal outcomes.

The data was calculated from 9,969 women without previous symptoms of hypertension and who were fewer than 16 weeks pregnant. The women were randomly assigned to receive 1000 mg of Vitamin C and 400 IU of Vitamin E or a placebo. The outcomes investigated were pregnancy related hypertension, eclamptic seizure, preterm birth and maternal or perinatal death. Results confirmed that vitamins C and E did not significantly reduce the risk of hypertension; the relative risk of the vitamin group was 1.07.

While other studies had previously suggested the role of vitamin C and E in lowering rates of hypertension in pregnant women, recent studies have not been able to reproduce this result. Most of the women in the trial were already taking prenatal vitamins, so many researchers suggested that the extra supplements were superfluous to normal levels of vitamin C and E.

Reference: *NEJM* Volume 362:1282-1291

The Future of Medical Imaging

Mark Leiserson

Medical imaging has played a major role in clinical diagnosis and treatment for years, allowing doctors to examine specific sections of the human body without resorting to invasive surgical procedures. Techniques such as radiography, magnetic resonance imaging (MRI), positron emission tomography (PET), and ultrasound have changed the way medicine is practiced. And they are just the tip of the iceberg when it comes to what is possible (or nearly possible, at this point) through the development of new medical imaging technologies. The increasing popularity of teleradiology and telemedicine, the widespread use of computer-aided diagnosis (CAD), the increased quality of current medical imaging technologies, and the development of new medical imaging technologies—specifically in the field of molecular medical imaging—seem certain to reshape the medical landscape once more. However, with these new technologies and practices come daunting challenges that must be overcome.

Traditionally, the utility of medical imaging has been strictly in-house diagnosis and treatment: technicians took an image, radiologists examined it and presented their conclusions, and then the image was archived. If a patient was undergoing long-term treatment, the image could be retrieved a few weeks or months later to be used as a reference to chart a patient's progress.² For many years, these medical images were taken and stored on film, though that has changed over the last two decades. The 2009 American Recovery and Reinvestment Act has catalyzed the process of digitizing medical records—including medical images—by providing \$19 billion in financing, but as of late 2009, “less than 10 percent of U.S. hospitals have adopted electronic medical records even in the most basic way.”³ As a result, many medical images are manually catalogued and retrieved, a costly process, especially considering the additional educational and administrative uses of medical images such as “teaching a trainee, producing a formal report, [or] justifying an examination to a third party.”¹

Despite the low rate of hospitals with electronic medical records (EMRs), some doctors have already begun to take advantage of having electronic medical images. Teleradiology is but one example. Teleradiology is the digital sharing of medical images between radiologists for the purpose of collaboration or interpretation, and has already been of enormous benefit to patients. An example of the use of teleradiology might look like the following:

“two patients arrive in the emergency department of a Maine hospital at midnight. The first has a presentation consistent with pulmonary embolism; the second, appendicitis... Today, both of these patients and hundreds of others like them would receive

middle-of-the-night CT scans, taxing the hospital's radiologists. But midnight in Bangor, Maine, is 10:30 a.m. in Bangalore, India. There — and in Switzerland, Australia, and Israel — sit teams of radiologists ready to read the scans and fax their findings back to the United States.”⁴

This practice has already caught on throughout the U.S. As of 2007 (the most recent year for which data are available), 44 percent of U.S. radiology practices utilize external, off-hours teleradiology services (EOTS).⁵ Teleradiology has the potential to improve patient-care even further, by transmitting medical images to those with subspecialty expertise, allowing patients to have the “most appropriate faculty” review images, regardless of geographical boundaries.⁶ As the digitization of medical images continues and transmission speeds of large images improve, look for teleradiology to expand even further.

A related field that seems poised to expand is telemedicine. Telemedicine is simply the interaction of doctors and patients through videoconferencing, sometimes coupled with medical imaging devices. Telemedicine offers the ability to decrease the cost of healthcare delivery and increase access to care—especially in rural communities—by allowing patients to “access expert care that might otherwise be unavailable,”⁷ thereby improving quality of life.

Computer-aided diagnosis (CAD) is a fast-growing research field at present that offers a way to make medical image interpretation much more efficient. CAD works by using different learning software to compare new medical images to past ones that have already had abnormal markers or lesions identified by radiologists. The software then reports its conclusions as to whether the new medical image contains an abnormal marker or lesion, and this conclusion is used as a “second opinion” by a radiologist. CAD has already been successfully implemented for a number of different cancers including breast, lung, and melanoma, as well as vertebral fractures and intracranial aneurysms.⁸

The future of CAD software most likely lies in software packages that will be incorporated directly into the viewing display of radiologists. Thus radiologists will be able to view the “CAD opinion” and relevant statistics concurrently with the medical image in question. Related or similar images can be linked to the viewing display as well, allowing radiologists to instantly examine past conclusions of similar images. In addition, there has been recent progress in developing CAD that would differentiate between diseases or between benign or malignant lesions or markers, rather than simply identifying

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“44% of U.S. radiology practices utilize external, off-hours teleradiology services.”

lesions or markers. Some researchers even believe that the software packages will be web-based, allowing a radiologist to simply upload a medical image and then have the areas of concern highlighted.

The improvement and increased portability of current medical imaging technologies will probably be the most widespread and transforming development of medical imaging in the near future. As has been the case throughout many fields in the 21st century, the continually decreasing cost of electronics has allowed devices that were once reserved for hospitals, CT scans for example, to move into medical practices. Cheaper and more portable new technologies are emerging to compliment tried and true methods. TechEn's Continuous Wave 6 (CW6) provides an example.⁹ CW6 is a quarter of the cost of an MRI and takes up less than 30 square feet (as opposed to the 300 square feet of an MR-Imager), which makes it extremely useful in situations where "portability and frequent follow-up measures are called for."⁹

Increases in resolution and quality of medical images are likewise expected to continue. For example, CT scans will continue to improve their "slice counts," allowing for large volumes to be visualized in a single-pass.⁹ This allows for faster CT scans, but also higher image quality. The fields of 3D medical imaging and molecular imaging are also expected to develop and grow, largely thanks to technological advancement. 3D medical images allow "clinicians to view high quality 3D images in real time and help them make clinical decisions with accuracy."¹⁰ Advances in molecular medical imaging will expand imaging probes to target "all the body's major systems and associated disease types," and will also be used to determine the effectiveness of certain drug treatments before they are administered.¹¹ For example, "radiopharmaceuticals will be used to create diagnostic images which visually indicate whether cancer patients are susceptible to multi-drug resistance."¹¹

With the promise of future medical imaging comes significant hurdles yet to be overcome. First and foremost is the issue of the electronic transmission and sharing of medical images, both within hospitals, to different domestic hospitals, and to different hospitals around the world. Electronic transmission of medical images is vital to teleradiology, telemedicine, and for certain CAD applications. During transmission, there are many opportunities for medical images to fall into the wrong hands, whether it be by human error or a network security breach. In the U.S., the unauthorized release of patient health information (PHI) is a federal offense, and therefore will require significant attention from both legal and computer experts.¹² In order for teleradiology, telemedicine, and remote CAD software to be realized, this challenge must be addressed.

The second major hurdle impeding the advancement of medical imaging is storage capacity and retrieval times of medical images. A CT scan image—as of 2008—could be up to 1GB, meaning that the retrieval of a CT scan within the same hospital could take up to 15 minutes.¹³ Furthermore, such large images, and the increasing rates and numbers at which they are being taken, presents a major storage problem.

The storage needs for medical facilities are growing by "at least 50 percent a year, with 60 to 90 percent of the storage capacity being consumed by image storage."¹³ In order to deal with this explosion in data storage requirements, larger and cheaper storage and greater network bandwidth is going to be required.

Despite these challenges, the future of medical imaging appears auspicious. Over the next decade, medical imaging technology will become more portable and produce higher quality images, and, coupled with the technology of the information age, will allow for the continued development of teleradiology and telemedicine. In addition, the continued study and refinement of CAD promises to improve radiologists' efficiency and accuracy in diagnosis. Just as in other fields, technological improvements are heralding in a new age in medical imaging. In the case of medical imaging, this change is sure to improve the diagnosis and treatment of patients, while reducing geographical barriers and overhead.

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BOOK REVIEW

Complications: A Surgeon's Notes on an Imperfect Science

Book by Atul Gawande

Reviewed by Kristin Bradley

Atul Gawande's *Complications: A Surgeon's Notes on an Imperfect Science* gives the reader exactly what is stated in the title: an insider's look at a relatively hidden and allusive profession. Through this collection of essays, Gawande reveals what actually occurs behind the operating curtain and in various other aspects of medical care. Through earnestly detailed descriptions, he gives a broad overview of the medical profession and its inherent imperfections in terms that are accessible to a diverse audience that includes both doctors and readers without a medical background.

Gawande writes from the well-informed perspective of someone who has experienced the trials and triumphs of medicine firsthand. He was a surgical resident at Brigham and Women's Hospital in Boston at the time of publication, and in the intervening years his career has skyrocketed. Among his many accomplishments, he has become a general surgeon at Brigham and Women's, served as an associate professor at Harvard Medical School, written for *The New Yorker*, and received a MacArthur Award.

Complications is divided into three distinct sections designed to show different aspects of the myriad problems faced by doctors on a daily basis. The first, "Fallibility," describes the rise and occasional fall of surgeons from the challenges of the learning curve during residency and the looming threat of burn-out that could lead to malpractice. The second and third sections, "Mystery" and "Uncertainty," both treat areas in which doctors do not have the expertise to correctly diagnose a patient or to find a cause for a diagnosis and how these problems are dealt with through a combination of new technology, new regulations, and educated guesswork. Gawande's writing is at its best as he uses his personal experience as fodder for his work, regaling the reader with compelling medical mysteries worthy of prime-time dramas. He artfully builds suspense to engross the readers while describing how doctors proceed from the presentation of symptoms to the implementation of treatment.

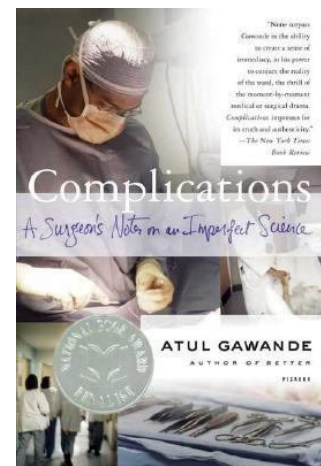
The essays clearly show the perspective of one individual, which humanizes the sometimes intimidating medical system. Although this personal touch can be informative, it can also be highly unsettling to patients who put their health in the hands of hospitals. In many instances, the guidelines that doctors rely on to proceed with a case appear to be unclear, such as the case of a man with chronic crippling back pain or a case in which the end-of-life decisions of the patient contradict the recommendations of their physician. In other situations, the ability of the doctor to make a judgment comes into question, as in the description of a renowned surgeon who overbooked his schedule and thus jeopardized the health of his patients. Attaching names (in most cases pseudonyms) and life histories to the situations makes each case more

personal, highlighting the central issue: how can doctors treat their patients perfectly when the doctors are imperfect?

The anecdotal evidence given to answer this question is covered in breadth but not necessarily in depth, which is appropriate to a book that gives an introduction to the world of medicine but leaves room for further investigation and expansion on topics. Topics vary from the preventable causes of malpractice, the relevance of autopsies in the future, and the new hour restrictions in residency programs all of which are still being debated with no certain outcome. Gawande provides a thorough introduction to different angles of these topics in addition to his own opinions on and recommendations about the matter, but the issues all merit further research into the current situation and the nuances of the debates.

Raising awareness and creating change seems to be one of the most important goals of the book. It is an example of modern-day muckraking, unflinchingly exposing the underbelly of medicine without pretensions. The triumphs of modern-day medicine are placed alongside its failures. Gawande admirably takes responsibility for his part as a cog in the complex machinery of medical decision making, describing both cases in which decisions he made led to the failure to save a patient and cases in which his decisions saved a patient against the odds. This convincingly conveys a full picture of such a precise science with unpredictable outcomes. The essays highlight the paradox of power in medicine; with the ability to save comes the inadvertent ability to do harm while struggling against the limits of scientific knowledge and technology.

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Complications: A Surgeon's Notes on an Imperfect Science

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Is Cosmetic Psychopharmacology Acceptable Medicine?

Paulina Zheng argues that anyone should be able to choose to take psychopharmacological drugs. Jeremy Nowak counters, suggesting their cosmetic use is ethically wrong.



Image www.communicationcurrent.com

YES The progress of science has made cosmetic psychopharmacology, or the administration of medication to improve personality and intellect, a conceivable possibility for the future of self-enhancement. However, the conception of cosmetic psychopharmacology inspires a new debate over the advisability of the use of such medications in psychologically healthy individuals.

Of course, society has always embraced the idea of self-enhancement. The societal emphasis on perfection has fostered the promotion of a myriad of procedures for the individual's convenience. The field of self-improvement is not new. Thus, cosmetic psychopharmacology only serves as a possible, albeit significantly life-altering, convenience for individuals in pursuit of personal change. Why, then, does the very idea of cosmetic psychopharmacology trouble critics?

Moral implications aside for the moment, critics also charge the potentially harmful side effects that

NO Imagine a drug with which, for a reasonable price, you could permanently alter your personality. You could be the individual you always wanted to be, constantly cheerful and always content with your well being. Just pop a pill every day and you could be the person you always dreamed of being.

No, this is not a pitch for the newest science fiction movie. This is reality in the form of cosmetic psychopharmacology, a phrase coined by Brown University psychiatrist Peter Kramer in 1990 when describing a then newly developed antidepressant called Prozac®.⁵ Cosmetic psychopharmacology “refers to taking someone from one normal, but less desired or less socially rewarded state to another normal, but more desired or more socially rewarded state,” explained Kramer.⁴ Drugs such as Prozac® are typically taken as prescriptions for individuals with emotional or mental disorders, such as depression or schizophrenia. However, there is an increasingly large number of individuals who believe that it should be legal for “healthy”

may result from the administration of psychotropic medication in healthy individuals. Such psychotropic drugs were only recently developed. As is frequently pointed out, the long term consequences of their use, even as intended, remain unknown by experts. However, it must not be assumed that the effects of current and future neuro-enhancing drugs will be unduly harmful to individuals before they are studied. Such drugs should be reviewed on a case by case basis, under the purview of the FDA. Given that the drugs are found to be safe for public consumption, why should these drugs not be accessible to the public?

It must also be noted that the societal emphasis on individual autonomy has led to the continued and legal existence of other drugs, such as tobacco and alcohol, despite their proven detrimental effects upon the individual's health. That is not to say that neuroenhancing drugs should be accepted, regardless of proven harm.

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individuals (those who fail to meet the criteria of any emotional or mental disorder) to use drugs such as SSRIs (selective serotonin reuptake inhibitors) and Prozac® to change their personalities. This concept is bioethically immoral and individuals should never take psychopharmacological drugs to permanently alter their brain chemistry or personality.

Drugs that alter the chemistry of the brain and thusly one's personality were not unheard of before the creation of Prozac®. Mental stimulants have been present in society in the form of nicotine and caffeine for centuries.¹ Coffee makes an individual more alert for a period of time, but the difference between these mental stimulants and SSRIs is that drugs such as Prozac® are viewed as “mental steroids,” as Christopher Altman puts it.¹ Prozac® alters cognitive functions by affecting the release rate of endorphins and of different neurotransmitters in the brain.¹ These drugs can potentially alter what the human population defines as a healthy mind, thus

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However, it is necessary to understand that the concern of critics on this point seems oddly misplaced, considering all the legal and validly harmful technologies and substances currently in existence as a consequence of the societal encouragement of individual autonomy.

Societal precedents would seem to suggest that cosmetic psychopharmacology should rightfully be considered as an acceptable means of self-enhancement. Critics such as Kass may argue that the effortless and appealing convenience of cosmetic psychopharmacology will result in the cheapening of identity by making everything too easy.⁵ However, as Chatterjee points out, this “no pain, no gain” mentality does not seem to have deterred society’s utilization of other conveniences and luxuries such as central air conditioning and Tylenol®.²

“Society has always embraced the idea of self enhancement.”

And what of modern innovations like liposuction? Society dictates that an individual has the freedom to make the decision to cosmetically enhance themselves; they do not require universal approval in order to undergo such a procedure. If they are unhappy about their appearance, they have the means to change their appearance in a way that satisfies them. If societal values allow this, then it can be argued that cosmetic psychopharmaceutical drugs should be accessible to the public. Society emphasizes autonomy and authenticity insomuch that authenticity can be pursued if individuals are permitted to be autonomous.

Contrary to critics’ assertions, authenticity is possible with cosmetic psychopharmacology.⁴ After all, psychotropic medications act upon what is already there. Current psychotropic drugs enhance the concentration of existing neurotransmitter molecules

in the brain. These drugs amplify existing, if hidden, personality traits. Rather than the creation of an artificial personality, the original personality is simply changed, without the possible restrictions imposed by less desirable characteristics.³ According to Bublitz and Merkel, “...it is patently implausible to consider traits originating from specific neurotransmitters, say serotonin, as not an agent’s own.”¹ As such, neuroenhancements do not replace a natural biological system with an artificial, alien system. They simply work with the pre-existing system.

It is also important to note that one’s identity is also subject to other environmental factors.⁶ Abuse and tragedy can repress and inhibit. Difficulty fosters depression. Psychotropic medications have the potential to remediate the oppression bred by external circumstances and allow the individual to experience their true identity, as nature dictated. Critics may still dismiss this as artificial on the aforementioned basis that pain “builds character, and eliminating that pain undermines good character.”²

it is better that they are only used to treat individuals who absolutely need them, rather than those who simply wish to “improve” their personality.

Mark Walters, a writer and researcher for CignaMedicare, explains that psychopharmacological drugs are supposed to improve the cognitive abilities of certain individuals suffering from conditions including depression and anxiety.⁶ Walters makes an excellent point when he states that the consumerism of these products displays the naivety of the general public and a general lack of understanding regarding how these drugs will affect a perfectly healthy brain.⁶ The average individual is never content with him or herself and wishes to change who they are. Companies can market drugs such as Prozac® by saying they will make you perfect, the person you always wanted to be. Philosophically speaking, a person should not feel the need to alter their personality using SSRIs because they believe they are inadequate or imperfect. Mankind is imperfect and that is perfectly fine.

An anonymous contribution to

Perspectives: A Journal of Reformed Thought examines cosmetic pharmacology from a theological and philosophical perspective. Even if one does not believe in a deity figure, the following sentence is difficult to argue against: “By using drugs to ignore pain’s warning signs, we would multiply our injuries and let disease go untreated, and so hurt ourselves far more severely.”³ One cannot simply take a drug to feel better about themselves; the individual will never mature or

learn from his or her mistakes. Creating an “alter ego” so to speak by fiddling with personality traits and emotional states is a gross abuse of medicine. These psychopharmacological drugs are to be used for sick individuals who lack other options. Prozac® should never be viewed as a different form of cosmetic surgery, except instead of altering one’s outer appearance it alters one’s inner appearance.

“Mankind is imperfect and that is perfectly fine.”

Being unhappy is part of life. Nobody should be happy twenty four hours a day, seven days a week. Individuals need to learn from sadness in order to mature and become better individuals. Everyone learns this concept when they are young, yet very few people choose to accept it. Victor

Reus, a professor of psychiatry at the University of California San Francisco, has stated, “My sense is that there are a number of people who may not meet the full criteria for major depressive disorder but are still experiencing dysfunction in their lives, and in addition, they just don’t experience pleasure in many different activities where they might have at one time.”⁴ These individuals can then hypothetically feel better about themselves by taking psychopharmacological drugs, but this action defeats the purpose of learning about oneself and finding what truly makes one happy. There are

OPPOSING VIEWPOINTS *continued*

YES

However, if an individual were in physical pain, no reasonable man would withhold a means to alleviate that pain from the individual on the grounds that 'it will build character.'

However, this source of alleviation will not, as critics do contend, be available to the general public. It is highly unlikely that psychotropic drugs will be an affordable option for everyone. But this does not mean a future reminiscent of Huxley's *Brave New World*. The creation of cosmetic surgery, after all, did not result in a significant aesthetic disparity between the wealthy and the poor. It is highly likely that cosmetic psychopharmacology will follow suit. This still does not mean that cosmetic psychopharmacology should not be offered as an option in the world of self-enhancement. It is still a plausible method of self-transformation.

It is society's responsibility to create a more equitable system that would not encourage such a distinction between the poor and the wealthy. This cannot be accomplished by merely withholding cosmetic psychopharmacology and other similar technologies from individuals.

It is important to consider possible implications and consequences in the cosmetic psychopharmacology debate. We cannot rush to accept it just because it looks promising. We must proceed with caution. On the other hand, we cannot hold back because we are afraid of this new technology. Progress is inevitable, essential lest our society fall into stagnation. Cosmetic psychopharmacology offers the opportunity for a new possible self, a new avenue in the constant pursuit of personal perfection.

NO

no "miracle drugs" that will make an individual content all of the time. The only way individuals can be happy is to take the time to find out what makes them happy, a method which no drug can ever replace.

Cosmetic psychopharmacology is one of the more bioethically immoral concepts currently present in the medical world. Bruce Charlton of the Department of Psychology at the University of Newcastle upon Tyne perfectly summarizes the purpose of these drugs: "These are drugs with the potential to give appetitive gratification, to give life more meaning. When they work, they are true 'happy' pills; where happiness is taken to be the legitimate goal of life."²

Physicians are not angels with the ability to grant happiness to any individual who asks for it. To be happy and content with oneself is the sole responsibility of said individual. If a person has a mental condition that requires a prescription dosage of Prozac® or another SSRI, then that is acceptable. However, a healthy but discontent individual should not rely on any form of SSRI to alter their brain chemistry or personality. Happiness cannot be purchased in a pill, thus it should not be legal for "healthy" individuals to use these drugs to change their personalities.

References for Opposing Viewpoints can be found online at TuftScopeJournal.org

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The Mental Health Parity Act of 2008: Why It May Not Benefit Those Who Need It Most

Sarah Moreland

The Mental Health Parity Act of 2008 was signed into law in October 2008. Under the law, a company that provides mental health benefits as part of a company health plan must provide them at parity with coverage for physical health services. Any deductible, co-payment or treatment restriction applied to the cost of treating a mental illness must be equal to that applied to a physical illness.⁴ While the law is a significant step forward, it has limited potential for helping those with severe mental disorders; the law excludes the homeless and unemployed, does not address the stigma associated with severe mental illness, and will benefit those with less severe mental illness more than those with severe mental illness. In order for the law to be effective in treating those with severe afflictions like schizophrenia and bipolar disorder, legislators must address the social stigma associated with severe mental illness.

INTRODUCTION

In a given year, 57 million people in the United States will suffer from a mental disorder. In fact, mental illness and addiction account for a higher percentage of lost work days than several common chronic physical conditions such as diabetes and asthma.¹ Although mental illness can cause great impairment, insurance companies have not historically covered mental illness to the same extent that they do physical illness; those who do suffer from mental illness are typically responsible for most of the co-pay or have to pay out of pocket.² During a 2002 Congressional hearing, New Jersey representative Marge Roukema aptly described the lack of insurance coverage for mental illness as analogous to “restricting diabetics so that they could not see their endocrinologists without enormous costs.”³

Although the gap between mental and physical health has been longstanding, many advocates for mental illness have fought for equal treatment. Senator Paul Wellstone and Representative Pete Domenici championed the Mental Health Parity Act of 1996, which prevented annual and lifetime limitations on mental health coverage. David Wellstone, son of Paul Wellstone, continued his father’s advocacy and was a significant proponent of the Mental Health Parity Act of 2008, which greatly expands upon its predecessor. The law establishes full parity between insurance coverage of mental and physical illness. The legislation is applied to companies with over 50 employees that offer mental health benefits. If a company meets these requirements, the law mandates that the company health plan must cover mental illness and addiction treatment to the same extent that it would cover physical and surgical health conditions.⁴

During an interview concerning the Mental Health Parity Act of 2008, David Wellstone stated that because of the law



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“there’s going to be equality.”⁵ While the Mental Health Parity Act of 2008 will undoubtedly increase access to mental health care, it will not create equality between physical and mental illness. This is largely because the law may not be effective in providing treatment to those with more serious mental illnesses such as schizophrenia and bipolar disorder, for several reasons. The law does not apply to the homeless and unemployed, a consideration as severe mental illness is disproportionately high in the homeless population. In addition the law does not address the social stigma associated with severe mental illness or prevent discrimination towards those with mental illness. Furthermore, the economic principle of moral hazard in conjunction with the low occurrence of severe mental disorders in the workplace will skew a company’s resources toward those with less severe mental illness. In order to be effective in treating the entire spectrum of mental illness, the law must address these concerns to truly achieve equality.

MISSING THE NEEDIEST DEMOGRAPHIC

When asked who will benefit from the law, proponent David Wellstone stated that the law “cuts across all lines, class lines: rich, poor, middle class, black, white, Asian, Hispanic,

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educated, non-educated [...]”⁵ While the law may greatly impact those seeking mental health treatments in the workforce, it disregards the unemployed and the homeless. A significant percentage of the homeless population suffers from severe mental illness and find it hard to pay for mental health care. According to the National Coalition for the Homeless, 6% of the general population suffer from a severe mental illness, whereas up to 25% of the homeless population suffer from a severe mental disorder.⁶ More specifically, according to the US department of Housing and Urban development, 664,000 people are homeless per night and of that population 26.3% suffer from severe mental illness.⁷ While some people are only briefly homeless, it is those with severe mental illness who tend to stay homeless. This specific population with severe disorders serves as an example of one of the worst possible outcomes when mental illness is not treated. Without treatment, those with severe mental illness cannot operate in daily life or fulfill their potential.¹⁰ While the act does mark a significant step forward in the progression towards equality for the mentally ill, it does not encompass a significant sector of society that could greatly benefit from the law.

The stigma associated with severe mental illness and addiction would prevent many homeless and unemployed people from gaining employment and benefitting from the law in any considerable manner. For instance, those with schizophrenia are often seen as dangerous and unpredictable.⁸ One study found that interviewers were less amiable and less likely to hire someone who had psychiatric hospitalization listed on their resume.⁹ In fact, homelessness may be the consequence of an untreated mental illness or addiction.¹⁰ David Wellstone has aptly commented that “a lot of that impact [of the law] is not even going to be seen cause again there’s so much stigma attached to mental illness and addiction.”⁵ Severe mental disorders such as schizophrenia and bipolar disorder can greatly impair a person in everyday life, to the extent that it is virtually impossible for them to maintain a job while being treated for their illness.¹⁰ As a consequence the law will not be effective in helping those with severe mental illness since attaining employment for those afflicted with these illnesses is difficult.

DISCRIMINATION WILL PREVENT PATIENTS FROM SEEKING HELP

The law will be ineffective in helping those with severe mental illness since it does not prevent the discrimination that the mentally ill experience, especially when seeking treatment. Namely, private insurance companies may deny coverage to a person because their mental illness could be classified as a preexisting condition.¹¹ In addition, many individuals with serious mental illness may not come forward fearing the repercussions if their current employers were to ever discover their disorder.⁹ So while the law mandates coverage for those with any kind of mental illness, fear of discrimination may prevent them from seeking treatment. Furthermore, the law only applies to insurance plans that are company-based.

Therefore a person could be diagnosed with a mental disorder as a result of seeking treatment through their company’s insurance plan and then later not be able to obtain coverage through a private provider because their mental illness could be considered a preexisting condition. Many who suffer from severe mental illnesses are painfully aware of the stigma and stereotypes associated with them and therefore are very careful about divulging that they have a mental disorder.⁹ Therefore those who suffer from severe mental illnesses like schizophrenia and bipolar disorder may not take advantage of the Mental Health Parity Act even if they are employed by a company required to comply with the law.

THE LAW WILL DISPROPORTIONATELY BENEFIT THOSE WITH LESS SEVERE MENTAL ILLNESS

Under the act, a company’s resources are more likely to benefit those with less severe mental disorders than those with severe mental disorders like schizophrenia and bipolar disorder for three reasons. First, as a consequence of moral hazard the use of mental health services will increase. Richard Frank is an economist specializing in the mental health economics. He defines moral hazard as “the tendency for people to demand more services as the price they pay for services falls.”¹² This phenomenon has been seen when companies expand their coverage of mental and physical health care; studies have shown that companies end up spending twice as much on mental health care than physical health care when the price of these services decreases.¹²

Second, severe disorders such as schizophrenia and bipolar disorder are rare in the workplace when compared to other disorders. Depression and anxiety disorders are typically less severe than schizophrenia and bipolar disorder since they are easier to treat. For example, major depressive disorder is encountered in the workplace at a rate of 6.4% where as bipolar disorder is only present in 1.1% of the working population.¹³

Third, general attitudes towards those with schizophrenia and bipolar disorder compared to those regarding depression differ greatly. People may harbor negative attitudes towards both depression and schizophrenia, but there is a difference in severity; while people often feel that depressed individuals are lazy and that they could easily do something about their disorder, schizophrenics are seen as dangerous.⁸ Since the mentally ill are aware of the stigma surrounding their condition,⁹ a person with depression may feel more comfortable seeking help than a person with schizophrenia. As a consequence the law will more strongly benefit those with depression and anxiety disorders because of the effects of moral hazard, the low prevalence of severe mental illness in the workplace, and the harsher discrimination towards those with severe mental illness.

MINIMIZING MENTAL HEALTH COSTS

Employee assistant programs argue that the Mental Health Parity Act can be enacted with minimal increase in

“A person with depression may feel more comfortable seeking help than a person with schizophrenia.”

cost if conditions are treated early. Employee Assistant Programs (EAPs) are commercial entities that aid companies in delivering a variety of behavioral services, including mental health care.¹⁴ ComPsych is an EAP that has successfully helped companies adopt the Mental Health Parity Act while decreasing costs. For instance, ComPsych helped a restaurant chain decrease overall behavioral health costs by 14.4% through its assistance. According to ComPsych, this was accomplished by treating the condition early in its progression and determining the appropriate level of treatment.¹⁴ This argument is not applicable to severe mental illness as these disorders are typically chronic in nature and require lifelong treatment. For example, a long term study with 104 schizophrenic patients found that rate of relapse after an initial episode was 81.9%, despite antipsychotic drugs. If the patient discontinued their antipsychotic medication, their risk for relapse increased five times.¹⁵ ComPsych also establishes a fixed number of sessions, which would not be effective in treating severe mental illness, as they often require lifelong treatment.¹⁶ Mental disorders have strong biological components¹⁷ and thus relapses into old patterns are likely to occur if treatment is only temporary. While preventative measures as modeled by EAPs can be used so that the mental health parity act will not increase costs, these strategies are not always applicable to those with severe mental illnesses.

NECESSARY CHANGES TO IMPROVE THE EFFECTIVENESS OF THE LAW

While the Mental Health Parity Act of 2008 will help many people suffering from mental illness, additional legislation concerning anti-discrimination and the scope of the law must be made for it to effectively help those with severe mental illness. The law has an economic focus, but in order for it to be effective, it needs to address the social aspects surrounding mental illness. For instance, the law must be amended to include anti-discrimination legislation; specifically it must prevent all insurance companies from characterizing mental illness as a preexisting condition. The law must also be expanded so that it aims to decrease the stigma surrounding mental illness within society. One option would include increasing awareness of mental illness through education. Schools could incorporate information about mental illness into the standard curriculum, allowing younger generations to accept mental illness and not propagate discriminatory attitudes. The law must also expand its scope so that it includes the homeless and unemployed demographics. Measures could include companies receiving tax discounts if they provide insurance for homeless people with severe mental disorders. Or perhaps companies could offer start up entry level positions to homeless people with severe mental disorders. Assuming these concerns would be addressed, it would provide a strong step towards true parity between mental and physical health coverage and bring significant upgrades in health benefits for so many in desperate need of aid outside of the current system.

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Polio Inoculation Gaps in Nigeria

Allison Marron

This paper examines the barriers to inoculating against polio in Nigeria and the difficulties it presents for the global eradication of polio. Without full population immunity against polio, a polio pandemic remains a real possibility. Poor education and ineffective leadership are two of the main difficulties groups face with immunization efforts in this West African country. Community level approaches and volunteer engagement are just a couple of the possible options to address vaccination difficulties. Establishing governance with organizations committed to international health, including the World Health Organization, the Global Polio Eradication Initiative and Rotary International will help Nigeria meet health goals and overcome this disease.

INTRODUCTION

The role of health in international relations is imperative because of its widespread effects on human beings in the global society. Inoculations have been used around the world to reduce the spread of many diseases and to reduce the threat of global health pandemics. Inoculations have been effective in eradicating diseases in many countries, in turn reducing the spread of disease to smaller areas. In areas where inoculations are not used heavily, however, certain diseases persist that threaten the unvaccinated population and neighboring areas, where disease could spread to again in future generations. The possible spread threatens these “safe” countries and the rest of the world as diseases cross borders in today’s globalized world. The main problems that prevent adequate, global inoculations are populations that refuse inoculations because of missing or incorrect information about the purpose of these vaccines, and insufficient cooperation of community officials. This paper will address education and consequential polio inoculation gaps in Nigeria, the threat they pose to global health, and the possible solutions that organizations could use to close these gaps and alleviate the threat of a polio pandemic.

THE POLIO DISEASE

“Poliomyelitis (polio) is a highly infectious disease caused by a virus. It invades the nervous system, and can cause total paralysis in a matter of hours. It can strike at any age, but affects mainly children under three (over 50% of all cases).”¹ Polio is easily spread because it can be transmitted through contaminated food and water sources as well as direct contact with an infected person. The first vaccine developed was the inactivated polio vaccine (IPV) in 1955, followed by the oral polio vaccine (OPV) in 1961. Currently the OPV is used most often in eradication campaigns since it is cheaper and easier to distribute.² Through the use of vaccines, polio has been eradicated in all but four countries: Nigeria, Afghanistan, Pakistan, and India).³

POLIO IN NIGERIA

Polio in Nigeria is especially problematic because of the international threat it continues to pose until the disease is eradicated. As of 2006, 60% of polio cases in Nigeria were documented in Northern Nigeria, particularly in the states of Jigawa, Kano, and Katsina.⁴ As is the case in Nigeria, “...where

routine vaccination rates are poor, poliovirus infection rates are high.”⁵ In 2009, 387 cases of polio were reported in Nigeria, out of a total 1595 global cases (approximately 24%).⁶

The barriers to vaccination in Nigeria had domestic consequences in the number of polio cases, and for that reason polio threatens the security of other states both regionally and internationally. “Not only is Nigeria struggling to contain its poliomyelitis outbreak, it is now exporting the virus across its porous borders.”⁵ When vaccinations stopped in Kano (northern Nigeria) from April 2003 to July 2004, there was a “...decrease in the OPV acceptance in all northern Nigerian states. The subsequent importation and re-emergence of polio is still haunting the world.”⁷ This “re-emergence” was the spread of the polio virus to neighboring countries, which the World Health Organization (WHO) attributes to Nigeria.⁸ In 2005, a strain endemic to northern Nigeria travelled to “Yemen, Saudi Arabia, and Indonesia (probably by Muslim pilgrims returning from the Hajj or migrant workers),” which paralyzed over 1,500 children.⁹ In 2008 this affected Benin, Burkina Faso, Niger and Chad.⁸

POLIO ON THE GLOBAL LEVEL

The spread of polio is a global concern. “International migration poses the threat of re-emergence and importation in the post-eradication era.”⁷ According to the Advisory Committee on Poliomyelitis Eradication (ACPE), “the continuing transmission of [wild poliovirus (WPV)] in northern Nigeria remains the main threat to eradication in Africa and globally.”³ Polio could easily spread internationally as tourists and professionals visit areas where the disease is present and bring it back to their home countries. Without eradication this spread is inevitable, especially since many countries that eradicated polio years ago no longer vaccinate against it. The population’s immunity to the disease would be low in these areas, making people more susceptible to infection. The root cause of this threat is low inoculation rates in Nigeria.

BARRIERS TO INOCULATION

The noncompliance of local leaders challenges inoculation efforts. In 2003, boycotts erupted in northern Nigeria, particularly Kano, against inoculating children with the polio

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vaccination. Local political and religious leaders urged parents to not vaccinate their children, and immunization campaigns ceased. “These leaders argued that the vaccine could be contaminated with anti-fertility agents (estradiol hormone), HIV, and cancerous agents.”⁹ Leaders believed that Western countries were targeting the Muslim world. A representative for the governor of Kano stated that, “Since September 11, the Muslim world is beginning to be suspicious of any move from the Western world...Our people have become really concerned about polio vaccine.”⁹ Margaret Cheng argues that the boycotts of inoculations were “fuelled by general resentment of the south and its political dominance of the country.”⁵ Power struggles between the north and the south explain her theory.

Although the federal government of Nigeria sets the national health policy, immunization campaigns are at the discretion of individual states, which allowed Kano to halt vaccinations in 2003.⁹ Discrepancies between northern and southern Nigeria are due in part to political changes to which the country is still adapting; in 1999, power shifted from “a northern-led military regime to a southern-led democracy.”⁹ Northern states boycotted polio vaccinations, believing that the democratic southern government was executing Western goals. Additionally, northern and southern Nigeria have “different attitudes to modern medicine,” partly because of their very different colonial backgrounds: Islamic Jihadists colonized northern Nigeria; the British colonized southern Nigeria.⁹ Southern Nigeria is more accepting of modern medicine, since British colonialists used more advanced medicine than Islamic Jihadist colonists in the north, who followed more traditional approaches to medicine.⁹

A great deal of opposition to vaccines came from common Nigerian citizens as well. In a country where medical treatment is hard to come by, and expensive when it can be found, free vaccinations appear to be a threat, rather than a miracle. According to a report for the *Baltimore Sun*:

*The aggressive door-to-door mass immunizations that have slashed polio infections around the world raise suspicions. From a Nigerian's perspective, to be offered free medicine is about as unusual as a stranger's going door to door in America and handing over \$100 bills. It does not make any sense in a country where people struggle to obtain the most basic medicines and treatment at local clinics.*⁹

Citizens also had similar concerns that immunizations caused infertility, but for different reasons. A population policy of President Babangida in the 1980's restricted women to having four children. Nigerians “connected this population control campaign with immunization, believing that vaccination was one way the government might be reducing the population.”⁹ These perceived threats caused parents to keep their children from being vaccinated.

Northern Nigerians are also skeptical of modern medicine because of bad past experiences. In 1996, Pfizer “sent a team to Kano during the epidemic of meningococcal meningitis.”⁹ Pfizer used that opportunity to set up a trial for new antibiotics; 100 children received the standard antibiotics used to treat meningitis, and 100 children were given the trial drug. Five children who received the new drug died. Claims were

made that Pfizer did not have permission to test the new drug, and that children who were not responding to the new drug were not switched to the standard treatment. There was little accountability for Pfizer's actions; US courts ruled that Nigerian families would have to file suits against Pfizer in Nigerian courts. Consequently, many Nigerians developed distrust for “Western interventions” and group vaccines in the same category as the Pfizer drug trials.⁹

Further, Nigerians view polio as less threatening than other diseases which are more visible and claim more lives. The “poliomyelitis vaccination is a long way down on the list of their needs,”⁵ compared to problems like measles, diarrhea and malnutrition, which claim billions of lives a year. “When the poliomyelitis vaccinators came [during the last measles outbreak] they said ‘go away’ we will only bring our children out if you bring measles vaccination,” explained Abdulsalam Nasidi, the Director of Public Health in Nigeria.⁵ People have little faith in the country's health system because of its inability to protect their children from common diseases. “[Parents] refuse to have their children vaccinated...because it is their only means of protest against a health system they feel is failing them.”⁵ Public health and vaccination efforts in the past have fallen short. In 2006 Nigeria introduced Immunization Plus Days (IPD) in which poliomyelitis and other vaccines were given to children, and insecticide-treated bed nets and soaps were distributed to parents. At first it seemed successful, since the number of polio cases declined over a year; it quickly turned around. “Poor planning, under budgeting, and procurement problems”⁵ caused the campaign to fall through on promises, and Nigeria regressed back to its 2006 level of progress against polio. For Nigeria to eradicate polio and alleviate the risk of a global polio pandemic, it is important that the Nigerian government, Nigerian citizens and international organizations take steps to cooperate to make this happen.

RECOMMENDATIONS FOR ERADICATION

To eradicate a disease it is important that a country has basic health services available to all of its citizens. Basic health services establish a framework for campaigns such as the IPD program. When there is accessible medical treatment, more people may pursue regular medical attention, and may voluntarily pursue vaccinations as well. This will also provide more comprehensive vaccinations by inoculating against common diseases, including measles, which parents are more concerned about than polio. Building a reliable health system also helps develop credibility and establishes public trust.

Public trust is essential in promoting public health. Such trust plays an important role in the public's compliance with public health intervention, especially compliance with vaccination programs, which targets mainly healthy people. Where public trust is eroded, rumors can spread and this can lead to rejection of health interventions.⁹

Establishing public trust will also help prevent future boycotts; when the public trusts the health system, they are less likely to be suspicious of motives of public health initiatives. Trust also comes from educating people about the health risks they face. Lahariya notes:

*The persistence of myths about polio, particularly in endemic areas, can result in low participation and poor cooperation...The solution may lie in including information on polio and vaccination in textbooks and curricula of school and colleges to generate awareness and increase people's participation in and ownership of the program.*⁷

Educating the population will inform people of the real health threats that exist, and that vaccinations are intended to protect their children, not sterilize them or infect them with HIV. Education will encourage parents to vaccinate their children against polio and participate in local campaign efforts. Local efforts will help facilitate governance between Nigeria and international organizations.

Confidence in community groups and local governments will be helpful in working towards eradication as well. Local governments are vital because they are closely tied to communities, and community based initiatives aid vaccination campaigns. In the past, "...poor community participation and insufficient ownership" slowed campaign progress in Nigeria.⁷ Further, "...social mobilization can be considered as important as political mobilization and both need immediate reinforcement."⁷ Volunteers are necessary to support local government campaigns and increase social mobilization. "...Volunteers know the community, its practices and beliefs, the terrain and the language of the area in which they work, facilitating the job of administering the vaccine with a high coverage."⁷ In other countries, eradication campaigns have been successful because of "the efforts of hundreds of thousands of people from different walks of life."⁷ According to the WHO, local efforts are crucial in vaccine campaigns. "Nigeria will continue to pose a high risk to international health until the new top political commitment is translated into field-level improvements in campaign quality."³

Local and state governments also require support from the international community. "Eradication should be an internationally coordinated effort" to guarantee the highest rate of efficiency.⁷ In the case of polio, "...many countries started programs in their territory a long time after a large part of the world was polio free. Had efforts been internationally coordinated and synchronous, the situation could have been different."⁷ International efforts would have provided equality for all countries by ensuring that each country was taking the same steps at the same time, and that financial support would be available to help countries eradicate polio. International efforts would also ensure accountability; one of the current problems in Nigerian campaigns is the misallocation of program funds: insufficient funds are allocated to projects, and funds are used improperly.⁵ As of 2007, the cost for global eradication was \$4.5 billion USD, and an additional \$575 million USD was needed to meet program needs. Coordinated international efforts would ensure that funds are used appropriately and that every country receives sufficient funds and would not have to rely solely on state resources. International support would also require better data collection, which Nigeria lacks. The UN or the WHO would be able

to help with census figures, tracking addresses and tracking which children still need to be vaccinated.⁵

To secure effective governance with international organizations, it is important that Nigeria cooperates domestically so that it can establish united national goals. It is crucial that northern and southern Nigeria reach an agreement on opinions of modern medicine so that one part of the country is not doing work that will counteract actions another part of the country is taking. This lack of communication was a problem previously, when ineffective vaccination campaigns in the north disrupted successful vaccination campaigns in the south. When the entire country is cooperating, Nigeria can establish effective governance by using local efforts to implement international goals. As Nigeria increases its effort, international organizations will take the country seriously and will be more willing to cooperate.

By working to meet the goals of external organizations, Nigeria will secure effective governance along the way. Organizations such as the WHO, the GPEI and Rotary International will see the continued value in aiding in eradication campaigns in Nigeria; when the country is accepting of the vaccines, international organizations will have an easier time with public compliance, and international cooperation between the organizations and Nigeria will secure governance among them. The GPEI, for example, could establish governance with Nigeria by promoting polio eradication goals. The goal of the GPEI is to "interrupt transmission" in the four polio endemic countries, including Nigeria.³ Nigeria must do this by achieving "consistent immunization of all children during [supplementary immunization activities]."³ The objectives of the GPEI are carried out by other organizations, primarily the WHO and Rotary International.

Governance can be established with the WHO when Nigeria takes steps to achieve the WHO recommended goals in poliomyelitis vaccination campaigns by consistently vaccinating all children during campaigns and "by addressing: the quality of campaigns (that is, the effectiveness of service delivery); the attitude and practice of the population in accepting or seeking out the service; [and] the ability of the service to gain access to all targeted populations, which is compromised in areas of uncertain security."³ Another necessary goal is that routine immunization should be used to maintain "high population immunity...in polio-free areas."³

Further, Rotary International and Nigeria can establish governance by using local and international Rotarian volunteers from the PolioPlus program to distribute vaccines to Nigerian communities and to vaccinate children directly. According to the WHO, "Rotary is the volunteer arm of the global partnership dedicated to ending this crippling disease."¹⁰ Rotary goals that Nigerians can work toward to secure eradication are to immunize infants with OPV, use National Immunization Days (NID), monitor for cases of acute flaccid paralysis (which indicates polio infection) and investigate them immediately, and go door-to-door to ensure that all children are vaccinated.¹¹

“Public trust is essential in promoting public health.”

CONCLUSION

It is important to maintain vaccination efforts in polio-free areas to keep immunity high. Once polio is eradicated in Nigeria, it must maintain population immunity by continuing to use the OPV for three years and the IPV for seven to eight years after that to guarantee continued eradication. True eradication takes approximately 10 years after the last polio case is documented to ensure that it is really gone.

Global polio eradication cannot occur until every country has been polio-free for 10 years. Until such time, as long as one country continues to report polio cases, the threat of a polio pandemic exists. Through global governance, however, this global health threat can be eliminated. The World Health Organization and Rotary International, through coordination with the Global Polio Eradication Initiative can establish effective governance with Nigeria by demonstrating coordinated efforts to achieve common goals. Nigeria can further contribute to governance through community programs and support from local governments. Comprehensive vaccination initiatives, paradigm shifts that accept vaccinations and continued vaccination campaigns to maintain high population immunity will push Nigeria to polio eradication, contain the spread of the disease, and alleviate this global health threat.

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NEWS AND VIEWS

Psychedelics Offering a Cure?

Like many Americans, Dr. Clark Martin, a clinical psychologist, suffered from depression. Dr. Martin fell into depression after chemotherapy for kidney cancer, and none of the traditional methods were helping him recover until, at the age of 65, he had his first psychedelic experience as part of an experiment at Johns Hopkins University, involving psilocybin, an ingredient in certain mushrooms. He claims this six-hour experience helped him overcome depression and entirely transformed his personal relationships. Similar studies using psychedelics have yielded encouraging results, but review boards have set up strict guidelines to avoid there being an exaggerated perception about the drugs' risks and benefits. However, despite positive results from multiple studies, there is still limited public money granted for psychedelic research, although nonprofit groups like the Hefter Research Institute have supported research efforts.

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A Decline in Death from Childbirth

Lower pregnancy rates, higher income (which correlates to better nutrition and healthcare), better education, and an increased prevalence of hospitals staffed with skilled workers have led to a worldwide decrease in maternal mortality rates. Improvements made in India and China stand out as major contributors to this development. In other regions, AIDS is a dominant factor in maternal mortality rates. These findings contradict the dominant view that maternal mortality rates cannot be combated. However, many advocates of women's health resisted the publishing of this data, fearing that the news would reduce public support for their cause. This opinion was contested by other medical professionals. Experts noted that public knowledge of this information demonstrates that public support and donation is having a positive effect.

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The Varicella Vaccine

Michael Cross

The United States of America became the first country to implement a mandatory, universal, childhood varicella vaccination program. This program specified a single dose for children between the ages of twelve months and twelve years. However, two years ago, the vaccination program was changed to a two-dose regimen because the efficacy of the varicella vaccine in producing immunity decreased noticeably with time. Concerns regarding the effectiveness of the vaccine, the potential for fewer, but more severe cases of varicella, and the increasing incidence of herpes zoster not only exist but also are especially serious. The potential for adverse effects brings attention to an important question addressing the implementation of any vaccination program: whether the taking of risks incapable of being calculated is worthwhile if there is clear potential for adverse events.

The United States of America became the first country to implement a mandatory, universal, childhood varicella vaccination program on May 1, 1995.⁶ This program specified a single dose for children between the ages of twelve months and twelve years.^{13, 15, 9} Two years ago, the vaccination program was changed to a two-dose regimen because the efficacy of the varicella vaccine in producing immunity decreased noticeably with time.¹⁵ Concerns regarding the effectiveness of the vaccine, the potential for fewer, but more severe cases of varicella, and the increasing incidence of herpes zoster not only exist but also are especially serious.^{15, 6, 12}

The potential for adverse effects brings attention to an important question addressing the implementation of any vaccination program: whether the taking of risks incapable of being calculated is worthwhile if there is clear potential for adverse events. Andrew Farlow, a research fellow at Oxford University notes that the decision to implement obligatory childhood immunization for varicella depends on many complex factors that affect each other including societal attitude, political atmosphere, economic state, scientific understanding, and individual interest.⁴ One must ask to what point is it even acceptable to implement a vaccination program without knowing the long-term consequences of the vaccine. A vaccination regimen should be implemented when the vaccine can have a positive impact on the overall health of society both immediately and in the future.

One of the most common communicable diseases in the world, varicella, commonly referred to as chickenpox, is caused by the varicella-zoster virus (VZV).^{2, 5} Most individuals over the age of sixteen remember chickenpox “as a normal passage of childhood.”¹ Before the vaccine program, it was estimated that four million cases of varicella occurred every year in the United States. Most of these cases occurred with individuals under the age of fifteen years, with children between the ages of four and ten years having the highest rate of incidence.¹⁰ This high incidence among young individuals correlates with the age at which children begin to attend school and daycare in the United States. Furthermore, the peak age of incidence of the primary infection is less than five years of age, suggesting that the increased use of day-care and playgroups lead to greater exposure at a younger age.² VZV is extremely contagious and can easily spread to others. Therefore, it is recommended that an infected child be sent home from school

until the symptoms subside, usually about seven days after the appearance of the rash.¹⁵ Generally, a child infected with varicella would not need any additional treatment beside rest and maybe some ointment to alleviate the itch caused by the rash.² Thus, varicella is a common disease that in nearly all cases not life-threatening.

While the symptoms of most cases are alleviated within two weeks, there exist serious complications from varicella. The most frequent complications include infected skin and soft tissue, dehydration, pneumonia, and encephalitis.¹⁰ These complications usually require professional medical attention. From 1987 to 1995, it is estimated that 10,632 individuals were hospitalized each year as a result of infection with varicella. Children under the age of five years accounted for nearly half of these hospitalizations, and adults at least twenty years old accounted for about thirty percent. It is paramount to note that “compared with varicella-infected children aged 5 to 9 years, infants aged < 12 months and adults aged ≥ 20 years had 6- and 13-fold higher risks, respectively for hospitalization.”¹⁰ More than two thirds of the patients who were hospitalized were otherwise healthy, and “only 11% had immunocompromising conditions.”¹⁰ Moreover, from 1970 through 1994, an estimated one hundred five patients died annually, and varicella was a contributing factor in at least forty more deaths per year. During the four years prior to the implementation of the varicella vaccine in 1995, individuals of at least twenty years of age “had a 25-fold higher risk for death from varicella compared with children aged 1-4 years,” and “89% of varicella-related deaths among children and 75% among adults occurred in individuals who were not immunocompromised.”¹⁰

It is clear that the varicella-zoster virus is a highly contagious disease responsible for at least one hundred deaths each year in the United States and that the cost of the hospitalizations due to complications arising from varicella is tremendous. However, knowing that there always exist serious risks in deliberately altering the epidemiology of a disease, one must ask whether there is a real need for a vaccine. Moreover, it has been proven that “recovery from the primary infection results, in most people, in life-long immunity to exogenous

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infection.”² After an individual is infected with VZV, the virus remains inactive in the dorsal root ganglia.⁵ Studies have also shown that re-exposures to varicella-zoster throughout life aid in the maintenance of effective immunity.² VZV causes both varicella and zoster, commonly known as shingles. This secondary infection, usually occurring when immunity has been weakened “is believed to result from reactivation of latent VZV, latency having developed during a prior attack of chickenpox.”⁷ Epidemiological data from the Brisson study in 2002 has confirmed that prior exposure to varicella builds immunity against successive zoster infection.² Thus, it remains debatable that the varicella vaccine is necessary if infection from the natural virus causes life-long immunity. Moreover, serious concerns that a significant decline in the incidence of varicella will put previously infected individuals at a much greater risk for serious complications due to a reactivation of VZV.

However, in May of 1995, the Food and Drug Administration (FDA) approved Varivax® (Oka/Merck), and the live attenuated varicella vaccine became commercially available.^{6,3} The vaccine strain was developed by Michiaki Takahashi at Osaka University in Japan in the 1970s.^{1,8} The initial varicella strain was taken from a Japanese child named Oka who was otherwise healthy. The virus was then passed through human embryonic lung fibroblasts, after which the strain was passed through guinea pig embryo cells. The virus underwent a total of about thirty-five passages.⁷ Since there is no animal model acceptable for the testing of VZV, the vaccine strain was initially tested in healthy children susceptible to varicella.⁷ Upon testing, no skin lesions appeared on those who were injected, but antibodies that develop with the natural virus developed with the vaccine strain as well as cell-mediated immunity.⁷ Following the testing on children with healthy immune systems, immunocompromised Japanese children were vaccinated because they were at higher risk for complications from VZV. The results demonstrated that the vaccine was safe and effective in inducing the production of anti-bodies and cell-mediated immunity in both immunocompetent and immunocompromised individuals.⁷ With these major developments, controversy arose as the risks and benefits of the vaccine began to be scrutinized, and “investigators who believe that the potential benefits of this vaccine outweigh its potential risks have continued to test the vaccine in the United States since the late 1970s.”⁷

The Oka/Merck strain of the varicella vaccine went through clinical trials in the United States, and in 1995 experimental data demonstrated the vaccine more than eighty percent effective in preventing the development of and immunizing from varicella with the potential for adverse events next to none.³ In 1995, the Advisory Committee on Immunization Practices (ACIP) recommended a single dose of Varivax® for children twelve months to twelve years of age.¹⁵ Even though the vaccine was not proven to eradicate the incidence of varicella infection, the vaccination program was implemented in the United States. Those who were vaccinated but developed symptoms of varicella generally had milder symptoms.³

The American Society of Health-System Pharmacists recommends the vaccine for the following reasons:

“It causes a rash, itching, fever, and tiredness. It can lead to severe skin infection, scars, pneumonia, brain damage, or death. The chickenpox virus can be spread from person to person through the air, or by contact with fluid from chickenpox blisters. A person who has had chickenpox can get a painful rash called shingles years later...about 11,000 people were hospitalized for chickenpox each year in the United States...about 100 people died each year as a result of chickenpox in the United States.”¹⁶

Before the vaccine, millions cases of varicella had occurred annually. The fact that the mortality rate is about one hundred out of millions presents varicella as extremely benign.

Estimates of the economic impact are shown in “cost-benefit studies, which include both direct medical costs and the indirect cost of a parent’s lost wages, show that there would be a return of \$5.40 in benefits for every dollar spent on the vaccine.”³ That means that spending thirty-nine dollars on a single dose of Varivax® will produce an estimated return of two hundred ten dollars and sixty cents. In addition, at the time the vaccine was licensed, the economic situation practically dictated that men and most women with children work full-time and simply “could not afford to stay home for a week with a sick child even if they wanted to.”¹ Indeed, economic factors affected the decision to license the vaccine.

However, in 2006, the ACIP augmented its decision with the presentation of new evidence about the efficacy of the single-dose regimen. From its implementation in 1995 to 2006, eighty-nine percent of children nineteen to thirty-five months old had been vaccinated, and “varicella-related morbidity and mortality were dramatically reduced.”¹⁰ The United States observed a reported decline of eighty-eight percent in the rate of hospitalizations and associated costs as a result of the varicella-vaccine. Direct inpatient and outpatient medical expenditures declined over sixty million dollars.¹⁰ Adverse events occurring in those who had been vaccinated were reported 16,683 times to Merck & Co. More than fifty-five million doses of Varivax were distributed throughout the world.⁶ Although the coverage of the vaccine is high and the economic impact significant, the single-dose regimen was proved incapable of the complete prevention of varicella outbreaks.¹⁵ A review of the effectiveness of the varicella vaccine determined that “a higher degree of effectiveness is needed in order to interrupt transmission and to prevent outbreaks in settings with high contact rates.”¹³ Compared with those vaccinated with a single dose, individuals vaccinated with two doses developed significantly more antibody titers and had a “3.3-fold lower risk for breakthrough disease and higher vaccine efficacy.”¹⁰ Thus, in 2006, the ACIP recommended the implementation of a two-dose varicella vaccine regimen.¹⁰

The United States is one of the few countries in the world that have adopted the varicella vaccine in the program for universal immunization. Andrew Farlow presents major concerns regarding the implementation of universal immunization, beginning that “childhood immunization for varicella

zoster virus may shift the burden of disease to adults.⁴ The consequences of such a shift in the incidence of VZV would cause major problems since the mortality rate in adults is almost thirty times greater.⁴ In addition, “getting varicella as a child confers life-long immunity, but it is not yet clear how long vaccine induced immunity will last.”⁴ While the vaccine was licensed in Japan and Korea in 1988, “doubts about the vaccine’s long-term effectiveness delayed its entry in the U.S. market.”¹ Data from early trials suggested that immunity from one dose would last no less than twenty years; however, the one-dose regimen was determined insufficient in this capacity. Analysis of clinical observations demonstrated that only partial immunity lasted for “at least 8 years.”⁸ Moreover, it was not even eleven years after the implementation in 1995 that the ACIP altered its recommendation to a two-dose regimen. Thus, it is obvious that serious concerns for the efficacy of extended immunity to varicella are evident.

Understanding the relation of herpes zoster (HZ) to varicella is fundamental in determining the value of universal childhood immunization.⁴ Zoster affects an estimated one million individuals in the United States annually¹¹, and about fifteen percent of human beings have an episode of zoster in their lifetime.⁵ Zoster can be a result of a broad spectrum of factors, notably from a “natural decline in VZV-specific cell-mediated immunity”¹¹ and is caused by “reactivation of the varicella-zoster virus (VZV) after primary VZV infection.”¹² Herpes zoster, more commonly referred to as shingles, usually begins with “pain, itching, paresthesias (numbness or tingling), dysesthesias (unpleasant sensations), or sensitivity to touch (allodynia)”¹¹ and causes “acute and chronic morbidity.”¹² The most common complication related to zoster is postherpetic neuralgia (PHN)^{5,12} is experienced by about forty percent of zoster patients over the age of sixty.¹¹ Characterized by “constant, severe, stabbing or burning, dysesthetic pain that persists...sometimes years after resolution of rash,” PHN has no universally accepted treatment.¹¹

Reynolds et al. have concluded that “in theory, universal varicella vaccination has the potential to change the epidemiology of HZ. However, to date, the data available in the United States do not provide conclusive evidence that such a change is occurring.”¹² On the other hand, studies have given evidence that zoster develops by “retrograde transport of virus from ganglia to skin in a host partially immune to VZV.”¹¹ Moreover, studies have reported that “exposure to people with varicella disease is associated with a lower risk of HZ.”¹² Nevertheless, accurate calculation of the impact of the vaccine is extremely difficult because separating the effects of the

varicella vaccine on the epidemiology of HZ is next to impossible. However, until these factors can be accounted for “we cannot adequately assess the possibility of additional effects from a varicella vaccination program that are due to changes in opportunities for external boosting.”¹² It is entirely possible that “given that exposure to VZV boosts natural immunity, the decreased circulation resulting from a mass vaccination could potentially result in an increased number of cases of zoster.”⁵ When Merck & Co. was asked to comment on this theory, Dr. Gordon Douglas, a senior physician at Merck, maintained that “it was not known whether the vaccine also protected against shingles (herpes zoster).”³ As the incidence of HZ may significantly increase over the next fifty years, “the burden of the increased incidence of HZ may counteract most or all of the benefits of varicella vaccination.”¹² Thus, this theory that the incidence of varicella is inversely related to the incidence of zoster is definite cause for concern and must be carefully evaluated.

In most studies, it is reported that potential risk factors for vaccine failure have been identified, but findings remain inconsistent. Most pediatricians were skeptical about the efficacy and the potential for adverse events of the vaccine.¹⁴ Dr. Arthur Lavin’s query presents a major debate involving the decision to implement the vaccination program: “How can our profession accept a tremendous intervention in the epidemiology of an overwhelmingly benign disease, with little idea as to whether more harm than good will result in the long-term?”¹ Farlow poses the dilemma: “must we always wait for all the evidence we need before acting so that we will be judged, with hindsight, as having made the right decision? What if we can only know by taking actions that give us the natural experiment that will tell us the best policy?”⁴ The decision to implement the vaccination program pivots on “a complex mix of society’s attitude towards different risks, politics, and scientific understanding.”⁴

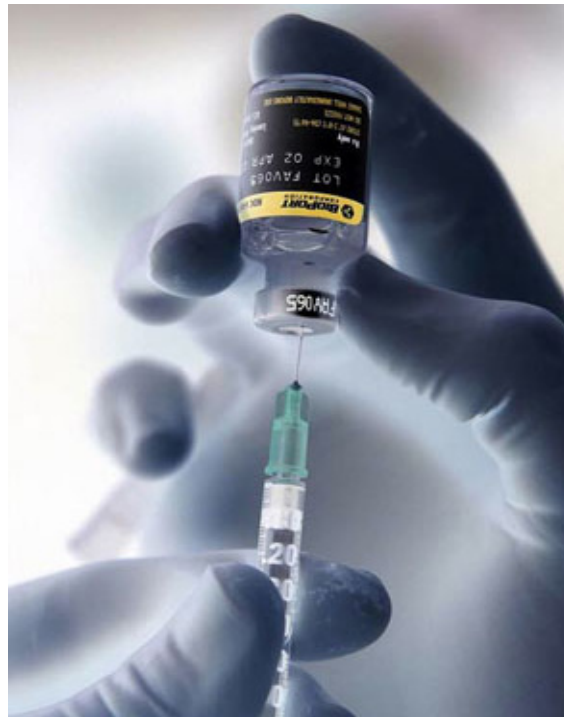


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Notes on Healthcare Reform

The 2009 – 2010 healthcare debate left an extensive paper trail in its wake. Volumes of articles, news stories, and blog posts were created to follow the daily developments that led to the passage of the Patient Protection and Affordable Care Act. It will take years for health policy scholars and historians to digest the full impact of the legislation. In the meantime, *TuftsScope* offers its annotated guide to the articles and multimedia presentations that the journal editors believe to be of lasting value:

General Articles

The Cost Conundrum

Dr. Atul Gawande tells the story of McAllen, Texas and the strange disparity in costs between the town and its neighbor, El Paso. This article became required reading in Washington, DC and promoted discussion of regional cost disparities in healthcare.

Gawande, Atul. “The Cost Conundrum.” *The New Yorker*. June 1, 2009.

Available online at: http://www.newyorker.com/reporting/2009/06/01/090601fa_fact_gawande

Making Healthcare Better

David Leonhardt recounts the efforts by Intermountain Healthcare (Utah/Idaho) to implement evidence based medical protocols throughout all of their hospitals. A struggle to realign medicine with its scientific roots.

Leonhardt, David. “Making Healthcare Better.” *The New York Times Magazine*. November 3, 2009.

Academic Works

The Obama Administration’s Options for Health Care Cost Control: Hope Versus Reality

A discussion on the options for cost-containment and a prescient picture of how far politicians were willing to go on reform.

Marmor T, Oberlander J, White J. *The Obama Administration’s Options for Health Care Cost Control: Hope Versus Reality*. *Annals of Internal Medicine*. 2009;150:485-489.

Available online at: <http://www.annals.org/content/150/7/485.full>

The Social Transformation of American Medicine

The seminal history through the 1970s on the origins of the modern American healthcare system.

Starr, Paul. “The Social Transformation of American Medicine.” USA: Basic Books. 1984.

Documentaries and Media

Frontline: Sick Around the World

T.R. Reid’s documentary on PBS travels to Japan, Germany, Taiwan, Great Britain, and Switzerland to examine how the rest of the world organizes its healthcare systems.

Reid, TR. “Frontline: Sick Around the World”.

Available online at: <http://www.pbs.org/wgbh/pages/frontline/sickaroundtheworld/>

Wendell Potter on Profits Before Patients

Wendell Potter, a former CIGNA executive, shares his experiences in the insurance industry and relates some of the tactics used by the insurance industry to oppose healthcare reform.

Bill Moyers Journal. “Wendell Potter on Profits Before Patients” July 10, 2009.

Available online at: <http://www.pbs.org/moyers/journal/07102009/profile.html>

Rationale for Implementation of Dental Care into Existing Maternal Prenatal Care Standards

Michael R. Pace

Periodontal disease is an infectious, inflammatory disease that can be caused by infection from bacteria found to commonly exist in the oral bacterial flora. Genetics, early childhood contacts, certain systemic diseases, unhealthy behaviors, poor oral hygiene, as well as pregnancy can facilitate infection and/or progression of the disease. Periodontal disease is not uncommon among pregnant women and is correlated to adverse pregnancy outcomes, especially preterm birth and low birth weight neonates. Although there are guidelines in place for healthcare professionals to standardize prenatal care, there are currently no existing guidelines for prenatal maternal dental care. Studies have shown that most health professionals that provide prenatal care do not regularly incorporate oral examinations for pregnant mothers as part of standard prenatal care. Periodontal disease can be safely diagnosed, which could lead to positive effects on the outcome of her pregnancy.

Prenatal care is the treatment that a woman receives from a physician while pregnant until the time she delivers her baby. Generally speaking, a woman visits her doctor monthly during the first and second trimesters, biweekly during the third trimester up to week 36 and weekly from week 36 until delivery of the neonate. This results in a minimum of 13 visits to her physician during her pregnancy. Most often these visits are to a medical doctor that has specialized in obstetrics and gynecology. During these visits the overall health of the mother and baby are assessed. Blood, urine and amniocentesis tests are performed as needed. To determine the position and development of the fetus, medical imaging procedures—typically sonography—are performed. These visits assess the health of the mother but also educate her about known causes of harm to her or her baby.

In 1959 the American College of Obstetrics and Gynecology (ACOG) published the first edition of Standards for Obstetric-Gynecologic Services. This publication helped with the issues that stemmed from not having uniform practice guidelines. Later in 1983 ACOG, along with the American Academy of Pediatrics, published *Guidelines for Perinatal Care*. These guidelines are updated as necessary. The publication of *Guidelines for Perinatal Care* has provided a reference for obstetricians and gynecologists as well as pediatricians and other physicians that treat pregnant mothers and neonates.¹

Although much as has been written about prenatal care, there is almost no mention of assessment of oral health or dental care during pregnancy in current guidelines for health care providers. Authoritative websites such as www.women-health.gov, which is maintained by the US Department of Health and Human Services Office of Women's Health, and www.medem.com, whose page on prenatal care bears the seal of the ACOG, do not even mention a dental exam nor recommend dental care for existing disease of the oral cavity.^{2,3} *Guidelines for Perinatal Care*, 5th Edition discusses topics that should be discussed between the physician and the expectant mother such as avoiding hot tubs and saunas and exercise guidelines.⁴ While these guidelines should not be omitted, numerous studies have shown correlation between poor oral health, specifically mothers with periodontal disease, and adverse pregnancy outcomes. Possible complications linked

to maternal periodontal disease include preterm delivery and/or low birth weight of the neonate. Poor periodontal health is correlated with complications in pregnancy and therefore dental exams and treatment should be implemented as an important part of maternal prenatal care.



Figure 1. Healthy gingival tissue. Source: Dr. Eric Vogel D.D.S.

PERIODONTAL DISEASE

Periodontal disease is an infectious, inflammatory disease of the gingival tissues that is caused by a bacterial infection in the oral cavity. Left untreated it will progress and can become the cause of many oral and systemic problems.

The gingival tissues (gums) surround the teeth. Healthy gingiva will lie slightly onto the anatomical crown of the tooth. This means that only the hardened enamel of the tooth is exposed to the sometimes harsh environment of the oral cavity. The periodontal ligaments, which hold the root of the tooth in the alveolus (tooth socket), are not exposed when the gingival tissues are healthy (Figure 1). The gingival sulcus is a gap where the gingiva meets the crown of the tooth. This creates an anaerobic pocket ideal for plaques and biofilms of disease-causing to colonize if proper hygiene is not practiced.

Causes of periodontal disease

Periodontal disease begins in the gingival tissues and can result in tooth loss. (Figure 2) As such, the aforementioned

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bacteria are the culprit for the disease.

These bacteria are usually the most malicious under the correct conditions. Factors including the ability for bacteria to form plaques and deposit on teeth, genetics, disease, early childhood contacts and unhealthy behaviors⁵ contribute to acquisition of periodontal disease. Pregnancy can also be considered a risk factor.

When periodontal disease causing anaerobic bacteria are able to settle in the gingival sulcus where there is less oxygen, the bacteria thrive and cause disease in the gingiva. Proper oral hygiene practices, especially flossing, minimize the effects of these bacteria.⁵

Genetics and predisposing diseases each play a role in the development of periodontal disease.⁵ Some diseases can be considered causative factors or at least facilitate the progression of periodontal disease in a myriad of ways. In the case of diabetes, vascularity in the oral cavity is compromised and the tissues do not receive the oxygen they need. In the case of other diseases the immune system is compromised making it difficult to fight off infection. A common side effect of many prescription medications and radiation therapy in the cranial region is xerostomia (dry mouth). Without the protective effects of saliva, the mouth is left very vulnerable to infection.⁵

Early in life the bacterial flora of the oral cavity is determined. If a child is exposed to malicious bacteria early in life it can have lifelong effects. Bacteria introduced from close contact between an infected mother and her newborn child often will colonize the newborn's mouth becoming a permanent part of the oral flora,⁵ thus increasing the likelihood of periodontal disease later in life.

There are many unhealthy practices that can promote the onset and development of periodontal disease. The evidence that smoking is causative of periodontal disease is longstanding and replete. Alcohol and other illicit substances such as methamphetamine can also lead to periodontal disease.⁵

Pregnancy can also serve as a risk factor for degeneration of oral health and periodontal disease. Pregnancy brings an abundance of changes in a woman's life. Diet is one of the more obvious changes. Food intake increases especially in the form of snacking rather than three established meal times each day. These new eating habits can be the cause of decay because of the excess food particles, especially sugars, remaining in the mouth. In many cases oral hygiene practices, such as more frequent tooth brushing, do not change to compensate for these newfound eating habits, thus leading to decay and/or infection. As the bacteria metabolize sugars an acidic byproduct is produced. Increases in acidity in the oral cavity may also be due to increased vomiting and acid reflux associated with nausea gravidarum. Decreased oral pH allows for demineralization of tooth enamel leaving teeth vulnerable to decay and infection. The decline in oral health during pregnancy is caused due to new eating habits and decreased pH in the oral cavity due to indigestion and morning sickness and which can increase a woman's risk for periodontal disease.⁶

Frequency of periodontal disease

In 1999 the *Journal of Periodontology* published a study

that stated at least 23% of women between the ages of 30 and 54 have periodontitis (a severe form of periodontal disease).⁷ The US Census Bureau has shown a trend that women are having their first child at an average age of 25.2. This is four years later than the average age in 1970.⁸ Risk of periodontal disease tends to increase with age. A significant portion of women of childbearing age are at risk for or currently have periodontal disease. If the current age trends continue to increase for age of first pregnancy, it is likely that periodontal disease will become a greater factor in pregnancy outcomes.

CORRELATION OF PERIODONTAL DISEASE TO ADVERSE PREGNANCY OUTCOMES

Dr. Gary C. Armitage, DDS, MS, professor of periodontology at University of California, San Francisco School of Dentistry stated, "Opinion has nothing to do with it. There are convincing data that chronic infections have a wide range of effects on general health. Some trivial, and some not."⁹ The female reproductive system is not excepted from the list of systems that can be potentially harmed from periodontal disease.

It has been known for quite some time that infection in the oral cavity especially periodontal disease can be causative of systemic maladies. As early as 1891 WD Miller proposed, "...microorganisms or their waste products obtain entrance to parts of the body adjacent to or remote from the mouth."¹⁰ Miller's theory was not readily accepted in his day due to lack of scientific evidence to support his claim.¹¹ It was not until the 1990s that concrete scientific evidence was shown that there are linkages to periodontal disease and systemic illness.¹¹ The three most researched and understood linkages are to cardiovascular disease, adverse outcomes in pregnancy and respiratory illness, respectively.

Miller's theory, in essence, is the accepted mechanism of the development of these pathologies. Bacterial components as well as bacteria can enter the blood stream via the inflamed gingival sulcus. As they enter the blood stream "immunoinflammatory mediators" are also released, causing a possible inflammatory response in other locations of the body.¹²

Low birth weight due to periodontal disease

Low birth weight is defined as a birth weight of less than 2500 grams (5lbs 8 oz).^{13,14} Some of the first research to establish this linkage was done by JG Collins and colleagues in the early 1990s. Pregnant hamsters were subjected to a porphyromonas gingivalis infection in a site that was distant from the placenta to simulate the effects of periodontal disease. The results of their study were a 20% decrease in birth weight of the neonatal hamsters.^{15,16} Numerous human observational studies have occurred in recent years that show decreased birth weight in humans as well. Damage done to the placenta from bacteria as well as immune response can cause blood flow and nutritional deficiencies in the fetus.¹³

Preterm birth due to periodontal disease

Preterm birth is defined as delivery at or before the 37th week of gestation.¹³ The immunoinflammatory response outside of the oral cavity mediates preterm birth in several ways. This



Figure 2. Stages of periodontal disease (progressing in severity from left to right). Source: Dr. Eric Vogel D.D.S.

immunoinflammatory response can irritate the smooth muscle of the uterus to promote contractions. Cervical effacement (thinning) and dilation as well as rupture of the chorioamniotic membranes also occur as a result of the immunoinflammatory response.¹³ The combination of these events increases the likelihood of premature delivery of the neonate.

SUGGESTIONS FOR IMPLEMENTATION OF DENTAL CARE INTO PRENATAL CARE STANDARDS

The old adage “an ounce of prevention is worth a pound or cure” could not be truer in the case of periodontal disease. Periodontal disease is a progressive disease that takes careful monitoring, stringent personal oral hygiene practices, frequent visits to a periodontist and often eventual surgery to prevent further degeneration of the periodontal tissues and/or tooth loss. Adhering to tooth brushing and flossing guidelines as well as semi-annual dental cleanings and exams can do a great deal to prevent the development of these conditions.

Educating health professionals

A study published in the *Journal of Dental Hygiene*, conducted by Rebecca Wilder, RDH, MS and colleagues shows the disconnect currently in prenatal care and dental care. Her study included a survey sent to 194 obstetricians in a 5 county area in North Carolina. The results showed that only 22% of the obstetricians in the study looked in their patients mouth at the first prenatal visit, a miniscule 9% periodically looked in their patients mouths on a regular basis and 48% looked only when the patient made mention of a problem. Only 51% of respondents in this study recommended a dental exam to their patients.¹⁷

Though obstetricians are neither trained nor qualified to accurately diagnose periodontal disease the fact that such low numbers in this study even looked inside their patients mouths shows there is not much attention given to the seriousness of periodontal disease in the pregnant patients among respondents to the questionnaire. The neglect of the issue is also shown in the fact that only 51% of respondents recommended a dental exam to their pregnant patients¹⁷ In order to see improvement in the number of infants affected by maternal periodontal disease there must be more education given to all health professionals involved with prenatal care.

The prenatal dental visit

In order for maternal periodontal health to be properly assessed it is necessary for the mother to have a thorough dental exam early in her pregnancy. When asked the question, “Do you feel that it would be beneficial to assess oral health as part of prenatal care? If so what do you think would be the most appropriate procedure?” E. Barrie Kenney, BSc, MS,

FRACDS, professor and chairman of the University of California, Los Angeles School of Periodontics responded, “All pregnant women should have a comprehensive periodontal evaluation carried out by their Dentist.”¹⁸ When others of similar positions at other institutions such as University of California, San Francisco and Harvard School of Dental Medicine were asked the same question they also agreed in a similar manner^{9, 19} A survey of 1604 general dentists in Oregon showed that 91.7% felt that dental treatment should be part of prenatal care.²⁰

An appropriate time for an expectant mother to also have a comprehensive periodontal examination is after her first visit to the physician that will be providing her prenatal care. Caution should be taken to ensure the pregnant mother and her unborn child are not exposed to excessive amounts of ionizing radiation in the dental office. A dental exam at this point allows proper time for diagnosis and treatment of periodontal disease if present.

Treating the pregnant patient comes with a unique set of challenges. Aside from the extra cautions that must be taken to avoid harm to the unborn child, comfort of the mother plays a large role in treatment choices. It is most comfortable for the pregnant mother if any necessary dental treatment takes place early in the pregnancy. During the latter stages of pregnancy changing body shape as well as sensitivity to the smells of the dental office and instruments in the mouth can prove to be challenges to providing treatment to the pregnant dental patient. The earlier the dental treatments take place during pregnancy, the easier it is for both the patient and the dental care provider.

Treating periodontal disease in pregnant women

Although there is not currently sufficient research to show that treating periodontal disease in pregnant women results in more favorable outcomes of pregnancy, there is nothing that shows that it is potentially harmful to the mother or her unborn child. The previously mentioned dental school professors and department chairs all feel that it is probable or possible that treatment of periodontal disease in pregnant patients would have favorable outcomes for the mother and fetus.^{9, 18, 19} When there is a good possibility that treatment of periodontal disease can have very positive effects on a mother and her unborn child and unnecessary risk is not taken, it makes logical sense to treat the mother’s periodontal disease.

Many dental procedures are completely safe for pregnant patients, however some are not. Radiographs should be avoided in pregnant patients. Consideration also must be taken in what analgesic and anesthetics are used during and after the procedure. Fortunately, there are suitable ways to treat periodontal disease in the pregnant patient.

The first step to treating any dental pathology is to correct the behavior that caused the pathology in the first place. The dentist should sit down with the patient and discuss with them what lifestyle and hygiene changes need to be made to stop/slow the progression of the disease.⁵

Scaling and root planning is a safe and effective procedure for treating periodontal disease. 96.9% of dentists in the Oregon study agree that scaling and root planning are appropriate treatment options for pregnant women.²⁰ This procedure typically requires no anesthetic and is not usually painful. There are also other treatments that can be performed by competent dentists that can prevent the progression of periodontal disease. Pregnant patients should discuss with their dentists all treatment options, including possible side effects and consequences of those options. Dental professionals should make sure to abide by the guidelines of informed consent before engaging in any dental procedure especially in a pregnant patient.

Perinatal considerations for mothers with periodontal disease

During the first few months of life an infant is making significant adjustments to their new surroundings. The first few months are crucial for immune system development and the development of the bacterial flora of the oral cavity. There are many complex factors that contribute to this flora that are beyond the scope of this paper. However, bacteria from the mouth of those who have periodontal disease can be introduced to the flora in the infant's oral cavity and implement itself into the developing flora. This can result in increased likelihood of the child developing periodontal disease themselves.⁵ For this reason it is important that during the first few months of life parents and others that will have frequent close contact with the child that have periodontal disease use caution to not introduce the disease-causing bacteria to the infant. This can be accomplished by those coming in frequent close contact with the infant with known periodontal disease using an antimicrobial mouth rinse.⁵ A competent dentist can recommend or prescribe an appropriate mouth rise.

The need for advocacy on periodontal disease and pregnancy

If changes to the current prenatal guidelines are to take place, measures must be taken to increase public awareness about the issues involved with periodontal disease and adverse pregnancy outcomes. Pamphlets must be produced that dentists can give to their patients. There must be opportunities for health care professionals (including medical and dental professionals) to increase their knowledge on the effects of periodontal disease and its systemic effects. Some of the necessary advocacy for this issue can be coupled with advertising for hygiene products that prevent or treat periodontal disease.

The prenatal dental exam will increase the cost of prenatal care. Work must be done with insurance companies and government health care assistance agencies to determine how these costs will be offset especially in low income patients. This should be quite achievable as it can be considered

preventative medicine that can possibly reduce costs of a high risk delivery and neonatal intensive care.

CONCLUSION

Periodontal disease is known to be correlated to low birth weights and preterm deliveries of newborns. As such, it is necessary that dental care is implemented into prenatal care. Prenatal dental care should include a complete periodontal examination as well as treatment for existing periodontal disease, if necessary. More research will likely show the effectiveness in improving pregnancy outcomes by treatment of periodontal disease, but it is logical to conclude that treating this disease will result in a favorable response.

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Cigarette Taxation Policies and Illicit Trade in the European Union

Piyali Kundu

Tobacco control advocates generally agree that taxes on tobacco products are the single most cost-effective policy tool to induce current smokers to quit, reduce consumption of heavy smokers and prevent uptake by non-smokers, especially youth.¹ The Framework Convention on Tobacco Control (FCTC), the first public health treaty negotiated by member countries of the World Health Organization (WHO), recognizes the importance of tax measures as “an effective and important means of reducing consumption by various segments of the population, particularly young persons.”² The goals of public health and those of fiscal authorities are seemingly in congress regarding the benefits of taxation on cigarettes.

However, the issue of how much and what kind of tax to levy depends on economic and political considerations and thus varies across countries and regions.³ This variance has economic and health implications for populations because it produces incentives for illegal cross-border trade that undermines the purposes behind the tax increases. For Europe, European Union (EU) tobacco tax harmonization – a process whereby all member states of the EU have brokered uniform tax rules for tobacco products – has produced a concerted regional effort to reduce the health effects of tobacco, increase revenue for governments and mitigate the criminal activities associated with tobacco trade for member states.⁴ However, comparisons among states and non-EU members highlight the complications produced by national tobacco tax policies that remain inconsistent with neighboring states despite harmonization efforts.

EUROPEAN UNION TOBACCO TAX HARMONIZATION

The European Commission (EC) has evolved its tax policy for tobacco over the past 20 years as more comprehensive approaches have become necessary to harmonize health policy on the issue of tobacco related morbidity and mortality. Due to the increasing number of countries entering the EU, harmonization has increasingly been a way to mitigate the risk between price differentials among states that causes illicit trade to flourish.

The structure of the EU tobacco tax is a unique blend of different types of excise taxes called the hybrid tax. It is a hybrid structure because it combines *ad volarum* and specific tax amounts to the overall excise tax, which is a percent of the total price of the pack of cigarettes. A specific tax places a standard, fixed currency amount imposed per 1,000 cigarettes no matter what the production cost and diminishes the differences between cheaper and more expensive brands. *Ad volarum* is a percentage of the value of the product, such as 45% of the manufacturers’ price. Value-added tax is levied on businesses at all levels of manufacture based on the increase

in price at each level of production. Combining these types to form a hybrid has served to gain consensus among member states that have different economic considerations vis-à-vis tobacco. In the 1980s, the European Commission (EC) pushed for common indirect tax rates to discourage smoking behaviour. This essentially meant a preference for uniform VAT tax as this is the consumption tax.⁵ However, the differences in prices between states barred this approach from coming to fruition and instead necessitated the current harmonization approach that sets minimum levels high enough to ensure revenues for governments and meet public health demands.

Since 1988, the EU Commission in charge of EU policy has stated that fiscal harmonization had to include an anti-tobacco component with uniform taxation rates that were “set at a level compatible with essential public health requirements.”⁵ Sticking true to the fiscal imperative argument, tobacco taxation policymakers of the EC had initially had the objective of raising revenue and protecting national manufacturers and growers. In 1992, there were several directives made to harmonize tobacco tax levels across all the member states. Also, because cigarettes and tobacco products have low price elasticity in that people addicted to nicotine will smoke regardless of taxes, there was potential to raise revenue for the member states and the EU. And lastly, the existence of negative outcomes, or externalities, due to increases in tobacco related morbidity and mortality meant that the revenue for taxes could offset the increase in healthcare expenditures.⁶

The initial proposal in 1992 produced price differentials across northern and southern EU states.⁶ The longer-term goal would be to impose a 57% *ad volarum* tax and a 0.43 euro-cent specific tax. However, these policies would result in a North-South divide. According to the EC there would be a 20% increase in expenditure on cigarettes across the EU because even as income rises, the demand for cigarettes does not change, leading to the conclusion that people continue to consume at their normal rate, leading to increasing expenditure on cigarettes (which means more profit for companies).⁵ Given the differential growth rates between Northern countries and Southern countries, Northern countries would have more expenditure on cigarettes that would diminish the impact of increased prices at the levels proposed.⁵ In the best-case scenario, policymakers posited a moderate decrease in consumption of 7% in all countries, but rising incomes would offset any decreases in expenditure on cigarettes.

The EU developed more robust levels of taxation to maximize the political leverage provided by the FCTC, which was signed by the EU in 2003. Under the auspices of the WHO,

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the FCTC calls for strong tobacco control measures from signatory states, especially high tax measures.⁷ Under the new policy, ad volarum taxes must be between 5% and 55% of the total tax on cigarette packs, reflecting the compromise with Southern member states that prefer the ad volarum taxes. Minimum excise tax – specific and ad volarum – must be 1.28 Euros per pack and the total level of excise tax must be 57% of retail price. When countries have only ad volarum taxes, producers can lower their prices because ad volarum taxes shifts according to the price of the product, whereas specific tax remains static. Placing the total level of excise tax as 57% of retail price means that producers cannot lower prices (i.e., switching to cheaper leaves, etc.) to an extent that will nullify the effect of the cigarette text.⁷

With these measures taken together, the level of taxation for cigarettes in the EU must be at a minimum of 70% per pack. Countries, however, are free to choose the proportion of specific versus ad volarum, as long as the minimum requirement is met. Ultimately, the harmonization process has set a standard for all member states and has increased prices in several states by a substantial amount. However, price differentials between states have not been significantly reduced, since member states can choose the proportion of specific and ad volarum to get to the 70% standard. This has led to intra-EU cross border shopping from high-price jurisdiction to low-price jurisdictions and to illicit trade between non-EU Border States and the EU.

SMUGGLING IN THE EU

According to experts in the Commission on Transnational Crime (OLAF), the office charged with spearheading the EU-wide response to tobacco-related illicit trade and tax evasion, the main concern for the EU is the large-scale tax-evasion and illicit trade of popular brand cigarettes that are sold in all states. The media and tobacco industry has instead focused on the local level cross border shopping between low tax and high tax jurisdictions as the main adverse result of taxes. Cross border shopping is legal within the single market of the EU and accounts for 3% of all cigarette consumption. The tobacco industry argues that tax differentials between neighbouring states leads to high rates in smuggling via this method, emphasizing cross border smuggling as the crux of the issue of illicit trade. Taking France as a typical, western European case study, cross border shopping constitutes 14% of all sales in tobacco as of 2006⁸ However, because of the Schengen agreement that allows unrestricted access across EU states, cross border shopping is a legal method of purchase, thus making it empirically difficult to measure just how much “smuggling” is done via this route.⁹ Thus, the focus has instead fallen on large-scale smuggling, sometimes called “container fraud.”⁸

A major shortcoming of the harmonization policies is the focus on destination-based taxes, which means that taxes are applied for a good at the destination countries – not at the country of origin or the port country⁸ The implication of this is a loophole that allows entrepreneurs, tobacco companies and organized criminal groups to circumvent the newly established taxation regimes.¹⁰ The kind of smuggling

this engenders is the main area of focus of the forthcoming, WHO-sponsored Protocol on Illicit Trade in Tobacco Products and the main area of work for the OLAF. Large scale smuggling consists of 7% of all consumption in Europe, with Eastern Europe leading the way with 13% of consumption.¹¹

In general, container fraud smuggling can be quantified by the difference in exports versus the volume of imports. The world production of cigarettes is known fairly accurately and thus it can be assumed that the production is equal of world consumption.¹² It is estimated that 586 million are imported each year, while 910 million are exported, with legal duty free sales accounting for about 45 million cigarettes. This means that over 300 million cigarettes are “lost” in the market.¹²

With focused attention on massive tax evasion as the main smuggling problem, OLAF says the direction of contraband cigarettes is from Western and Northern wholesale markets to non-EU states in the East, such as Ukraine and Serbia. From these countries, the cigarettes are either sold on the streets or imported clandestinely back to markets of the EU states (both North and South) where they do not pay any taxes.¹³ The direction of the trade is paradoxical and against the economic assumption that smuggled goods flow from low-tax jurisdiction to high tax jurisdictions – meaning from Eastern Europe to Northern/EU regions. This does not happen because buying cigarettes even from these regions would mean paying some kind of tax, which would not yield high profits. Thus, it is cheaper for smugglers to pay 0.30 euro cents wholesale price for imports in the Northern European ports, ship the goods to low-tax Eastern European countries where they would not have to pay high taxes, and smuggle back into western Europe and sell them for market value, duty not paid.¹³ The Schengen Agreement and the trade law that allows cigarettes destined for a European country to not pay any duties at the port of entry enable the exploitation of this route. Smugglers can easily re-route transport or forge documents to state that the end destination has been reached. In other cases, these cigarettes may actually be exported to Eastern Europe with large portions smuggled back via speedboat from Andorra, Cyprus, the former Yugoslavian countries, Albania and others.¹²

TOBACCO POLICIES OF EU BORDER STATES

Given the method of obtaining contraband cigarettes, the border EU states have remarkably high percentages of total consumption coming from smuggled chains as well. In Lithuania a packet of Marlboros costs \$2.00, making it the lowest priced jurisdiction in the EU. However, as of 2008, 36% of all cigarettes consumed came from illicit trade¹⁴ Conversely, in places like the Netherlands, Belgium and Denmark that have much higher prices for packs and over 70% tax incidence on the most popular brands, smuggling constituted 5% of the total consumption¹² The difference can be attributed, partly, to borders with non-EU states that have environments conducive for producing and importing cheap cigarettes, duty unpaid; links to organized crime that can enable smuggling; and smoke-friendly legislative environments that allow tobacco companies to profit from smuggling.

From the findings of crime investigators, tobacco control

experts and health economists, container fraud is supply-driven, related to organized crime, the culture of street selling and the complicity of the industry.¹³ The inability of harmonization thus far to produce blanket results is even more apparent when comparing the non-EU states that border the EU and the taxation policies therein. In the realm of trade and the movement of goods, the major ports of Europe are located in the EU – Rotterdam, Antwerp, Rostock and Hamburg – and goods move across via train to non-EU border countries daily.¹⁰ During negotiations between EU member states and newly independent states from the former Soviet Union, countries emphasized that what has worked in the developed countries of western Europe regarding tobacco taxation would not work in these developing states. The reliance on a strong civil society and a basis for non-governmental organizations to educate the public on the harmful effects of tobacco and the need for taxation was not a viable recourse for the governments.¹⁵ Likewise, the bureaucratic structure to implement taxation and ensure the transparent and effective transfer of revenues to different departments was underdeveloped compared to the evolved governments of the Western and Central European states in the EU.

The reality is that nearly half of the 6% of cigarettes sold with duty not paid (contraband) come from Eastern Europe, according to BAT, at \$85 billion in sales. Sales of contraband cigarettes are at 13% in Eastern Europe, compared with 7% in Western Europe (despite it being the highest priced region).¹³ This is due to environmental factors, such as lax legal regimes, need for foreign investment to boost new market economies, and easy access to lucrative markets in the West. In the interesting case of Andorra, the complicity of the industry is highlighted, demonstrating that taxes are subject to circumvention not just by criminal networks and entrepreneurs, but by the industry itself.

Andorra Case Study

BAT and Imperial Tobacco shipped upwards of 1520 million cigarettes to the small principality by 1997, increasing from previous shipments of 13 million. Unless Andorrans were smoking 60 British-brand cigarettes a day each, these excess cigarettes were smuggled back either to the United Kingdom, where they would have entered the black market or gone onto other destinations, duty not paid since packets would have “Andorra” as the destination.¹⁶ It was possible to conduct such operations in Andorra because of the lax rules regarding imports and exports and a strong organized crime base that would act as legal distributors of BAT and Imperial Tobacco products. Most importantly, Andorra is a tax-free zone, making it a tax haven for banks, customers and companies alike. Thus, the profit margin of conducting business through Andorra illustrates why this is such a lucrative business: a container of cigarettes, which has 5-10 million cigarettes, originating in the UK can be bought for \$200,000 and resold for \$2 million. Lost revenue for the UK government reached 2.5 billion pounds by 1997, even as industry officials collected their profits, since their money comes from the initial sale of the product.¹⁶ Manufacturers are technically within the law in such countries’ jurisdictions, because

they are separate from the handlings of dealers and retailers. Manufacturers of British cigarettes could sell these exorbitant amounts of tobacco to Andorra and not be required to follow up on where the end-market lay.¹⁶

POTENTIAL SOLUTIONS

As identified by the EC and OLAF, smuggling has gone from wealthier, high-tax countries to less developed, low-tax countries rather than the other way around. As explained above the main reasons for this have been: 1) EU trade laws that allow goods to be taxed at destination points, allowing companies to ship to countries where taxes are low; 2) smoke-friendly legal and business environments in non-EU countries such as Andorra allows companies to produce cheaply and in excess, fuelling the illicit trade; and 3) prevalence of criminal organizations that have networks reaching throughout Europe.

One main solution is to “turn off the tap” of supply driven tax circumvention by criminal organizations and the tobacco industry that are at the heart of the smuggling problem.¹³ Given their focus on domestic circumstances, member states often overlook the regional considerations necessary in staving off illicit trade.¹⁷ Giving into the fear mongering by industry officials, Sweden reduced taxes due to concern over smuggling after having two substantial tax increases in December 1996 and August 1997. The main reason was an overblown misconception that cross-border shopping would flood the Swedish market.¹⁶ Conversely, Spain has been one of the most successful in reducing smuggling despite having one of the cheapest cigarettes markets in the EU. Contraband from Andorra flooded the Spanish market to an extent that 15% of all cigarettes sold within Spain were duty not paid. Efforts between French, UK and Spanish governments and OLAF sealed off the Andorran border and civil guards were mandated to patrol hills and valleys to control smuggling at the “container” level (5-10 million cigarettes). These coordinated policing efforts decreased contraband market from 15% of all sales to 5% by 1999 without any change to the tax incidence of 76.1% on the most popular brand cigarettes.

Secondly, in order to mitigate the unintended consequences of the European trade law allowing taxes to be levied at destination points, a “track and trace” regime could label all products with the port of destination so that products cannot be diverted to illegal channels.¹⁸ An effective track and trace regime is a major issue of negotiation during the current intergovernmental session of the Protocol on Illicit Trade in Tobacco Products. Article 15.2 of the FCTC also highlights the need for the Parties to the treaty to set up effective measures to trace at which point products are directed to identify where the criminal activity originates.¹⁹

The harmonization policies also have issues of contention between public health and fiscal goals. In order to ensure that tobacco taxes meet the health objectives of decreasing prevalence and preventing uptake, taxes must be earmarked for tobacco control programs. Earmarking has been proven to multiply the beneficial health effects of increasing taxes, with examples from the United States showing that when even a portion of the tax revenues goes to anti-smoking activities,

decreases in consumption levels and prevalence are larger than expected.²⁰ Additionally, the issue of smuggling is recognized as an important public health issue as it introduces cigarettes at low prices all over the EU, threatening efforts to decrease prevalence and preventing uptake, especially by youth.¹³ One way to earmark taxes is to set up health promotion foundations that provide sponsorship to sports, arts and other organizations to replace tobacco sponsorship.¹³

Overall, the harmonization of tobacco taxes in Europe is a unique regional experiment in curbing the tobacco-related health outcomes by tackling the economics of tobacco. Additionally, harmonization in tobacco has been an experiment in setting regulations under the single market system where transport and trade are nearly borderless among countries within the EU and for most border states not in the EU. The battle now is to fine-tune this regime so illicit trade cannot undo its successes.

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NEWS AND VIEWS

Study Shows that Robots Can Aid Stroke Patients

A randomized trial has recently shown that rehabilitation assisted through the use of robots actually results in improvements in motor function and quality for patients who suffer from chronic disability following a stroke. *The New England Journal of Medicine's* researchers reported that significant progress has been observed in basic motor function. Time taken to complete everyday tasks for the robot-assisted group was at only 36 weeks, as compared with usual care. Albert Lo, MD, PhD, of the Providence Veterans Affairs Medical Center in Rhode Island, and his colleagues have cited that these findings "provide evidence of potential long-term benefits of rehabilitation and challenge the widely held clinical belief that gains in motor function are not possible for long-term stroke survivors."

Results demonstrated that compared with usual care, robot-assisted therapy was superior on one of the secondary endpoints, the Stroke Impact Scale, which measures quality of life and social participation. Certain criticisms have come up, however, such as that it might have been difficult to observe between-group differences because of the effects of certain patient characteristics, like depression. Nonetheless, "the potential for robotic therapy after stroke remains enormous," Steven Cramer, MD, of the University of California Irvine, wrote, noting that "robots never get tired, can design training regimens in reproducible ways, reduce the need for human oversight, can measure performance during therapy, and can provide simultaneous cognitive training by interfacing with computers."

Reference: Neale, Todd. (2010, April 16). Robots May Aid Stroke Recovery. *MedPage Today*.

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Addition to Chemotherapy Helps Survival Rate of Pancreatic Cancer

Data from a small phase I clinical trial shows that pancreatic cancer patients given an insulin growth factor (IGF) inhibitor combined with chemotherapy resulted in durable responses beyond one year. According to Rachna Schoff, MD, of M.D. Anderson Cancer Center of Houston, this data shows that "for a subset of patients, IGF-1 receptor is integral to pancreatic cancer." IGF type 1 receptor (IGF-1R) initiates signaling pathways involved in the pathogenesis and pathophysiology of pancreatic and other cancers: MEK/Erk and PI-3Kinase/Akt. MK-0646 is a human antibody against IGF-1R that leads to the receptor's internalization and subsequent degradation. Preclinical studies have shown that IGF-1R signaling increases the efficiency of chemotherapeutic drug. For this study, of the six patients who had partial responses, the shortest that was 14 weeks. The remaining five patients had response durations of 32 to more than 59 weeks.

Reference: Bankhead, Charles. (2010, April 26). AACR: Durable Responses Seen In Pancreatic Cancer. *MedPage Today*.

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Gee, What's GWAS? A Look at Genome-Wide Association Studies

Alan Hsu

With the advent of genome sequencing, and the development of technological methods to analyze genomes quickly and accurately, a new type of whole-genome analysis has emerged to analyze the contribution of genetic variation towards disease. Genome-wide association studies (GWAS) are a tool to understand complex diseases ranging from diabetes to lupus. At the root of the functionality of GWAS are the multiple polymorphisms shared within the human population and the extent and frequency which they appear in relation to the incidence of certain pathologies. By merging these fundamental aspects of biology with cutting edge technology, researchers have utilized GWAS to uncover potential mechanisms of disease, and in turn, potential pathways for treatment. This paper discusses both the background and the detail of genome-wide association studies and highlights their current role in the field of lupus research.

On April 15th, 2003, a consortium of leading scientists and academic announced that the human genome had been completely and accurately sequenced. In a conference headlined by Dr. James D. Watson, who fifty years earlier had helped discover the structure of DNA, scientists of the multi-institutional Human Genome Project revealed their findings: the total human genome, composed of 3.1 billion base pairs, 30,000 genes, at a cost of nearly 3 billion dollars.¹ Even in the decades leading up to its realization, the sequencing of the full human genome had been lauded for its potential in advancing both science and medicine. Now, with the entire genome sequenced, studies to realize these advances were being rapidly initiated.

Among the first studies, which utilized findings from the newly discovered genome, were those that attempted to discover the genetic basis of disease. With the entire genome mapped, scientists could now analyze the sequence to select a set of single-nucleotide polymorphisms (SNPs), which span the entire genome, and utilize these SNPs to assess genetic variation between individuals. Using these SNPs, researchers could analyze patients with complex diseases in order to shed light upon the genetic, and potentially the biochemical, causes of their conditions. In the ensuing years after the sequencing of the genome, an array of genetic studies analyzed a multitude of diseases ranging from schizophrenia to stroke.^{2,3} This research continues today where, six years later, whole-scale genome analysis still remains, both in methodology and applicability, very much in its infancy.

GENETIC BASIS OF DISEASE AND GWAS

The usefulness of SNPs stems from the commonality of the polymorphisms among individuals. 90% of all sequence variation within the human population is a result of the 10 million common SNPs that have been found in humans, an average of nearly one SNP per 300 bases.⁴ One specific nucleotide in the human genome sequence can take four possible "allelic" forms, corresponding to the four main nucleotide bases (adenine, cytosine, guanine, and thymine), but generally only two such bases become significantly present in the population, with one, generally the evolutionarily oldest, often becoming the most common variant. This single most common variant does not always have to be the SNP that

confers a survival advantage, and often it is the case that the second, largely benign, SNP, has arisen more recently out of random mutation and has become stabilized in the population over time.

Disease-causing mutations that have arisen from single nucleotide changes, often resulting in either nonsense or frame-shift mutations, could thus logically be considered a SNP. However, given that these "high-risk" alleles often limit the reproductive fitness of their carriers, they should remain rare variants over time. For these mutations, it is often the case that only one single nucleotide change is necessary to cause full clinical manifestation of the disease. One example of such a disease is the Wiskott Aldrich Syndrome (WAS), wherein one nucleotide change in the sequence coding for the WASP-interacting protein (WIP)-binding region of the Wiskott Aldrich Syndrome protein (WASP) can lead to full degradation of the protein and subsequent disease symptoms.⁵ Given the relatively clear mutation-to-disease correlation, genetic diseases such as WAS, with the potential for onset caused by one single nucleotide mutation, can be traced with relative ease through traditional linkage studies and hereditary analysis.

The ability for polymorphisms to cause disease is often measured by the "relative risk" (RR) of disease which the variation may incur, which is measured relative to the risk of disease found in the general majority of the population. Thus, if a polymorphism confers disease in 90% of its carriers relative to the 3% of disease in non-carriers then the relative risk would be 30. For diseases such as WAS, a SNP can have a tremendously high relative risk of disease, given that most of the individuals with one unique mutation can exhibit the symptoms of WAS. The capability of this particular mutation to effect disease can also be considered under its "effect size" or the scope in which one particular mutation contributes to disease onset and the penetrance of the particular mutation, which, in medical genetics, describes the proportion of people with the polymorphism which actually exhibit disease symptoms.^{6,7} Thus a SNP in WASP which disables essential WIP-WASP binding, leading to WASP degradation, would

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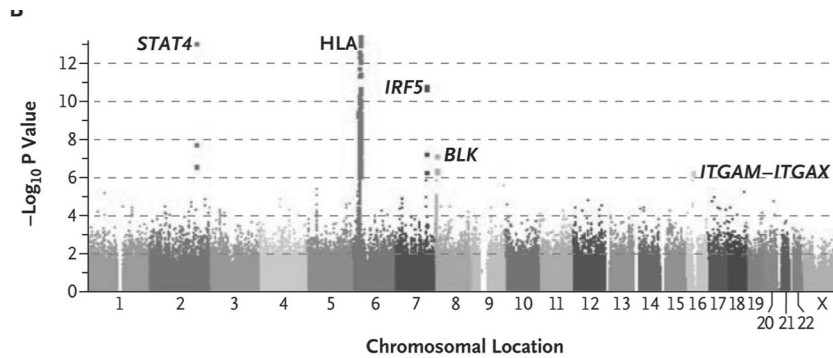


Figure 1. Identification of major loci associated with SLE in a GWAS of 1,311 SLE cases and 3,340 controls characterized for 502,033 SNPs. Adapted from 10.

have a very large effect size, confer a high relative risk of disease, and likely have very high penetrance within the population of its carriers.

But SNPs also operate subtly, contributing to disease with a small effect size and a small increase in relative risk of disease, often only 1.2 to 2 (hypertension and smoking confer similar RRs towards coronary artery disease).⁶ With such small effect sizes for individual SNPs, full disease onset can be dependent on multiple polymorphisms across multiple genes, each one conferring varying degrees of risk of disease. The subtleties of ascertaining the genetic bases of complex diseases thus confound the applicability of traditional linkage and hereditary analyses in researching these complex diseases. However, with the advent of genome sequencing, and the development of technological methods to analyze genomes quickly and accurately, a new type of whole-genome analysis has emerged to analyze the contribution of genetic variation towards complex disease. These genome-wide association studies (GWAS) are not unlike a fisherman casting out multiple lines, as they utilize complementary sequences proximal to the SNPs (the hooks) to identify SNPs (the fish) that may elucidate certain characteristics, and potentially the disease state, of a patient (the body of water). These complementary sequences, thousands upon thousands in number, are hybridized to microchips and used to probe subject DNA.⁶

The applicability of genome-wide association studies is grounded in the concept of linkage disequilibrium, which describes the association between multiple alleles at multiple loci within the genome. The importance for linkage disequilibrium (LD) arises due to the association between various SNPs in a certain region of the genome. Two or more SNPs with strong linkage disequilibrium are closely linked, often traveling together in blocks of genome sequence through inheritance and evolutionary history. These strong associations between proximal SNPs allows for the use of a tagging SNP to indicate any potential variation among all SNPs within a linkage disequilibrium block, which is often representative of a specific genomic sequence at that loci.^{4,6} Thus, while nearly 10 million SNPs are considered to be present in the human genome, strong linkage disequilibrium allows for the use of only a few hundred thousands tagging SNPs to identify trends in variation within the entire genome. Utilizing these tagging SNPs, GWAS attempt to identify variations in loci which may significantly contribute to disease. The majority of GWAS are case control studies, in which the DNA from a select group of afflicted patients and non-afflicted controls are taken and

probed for variation within the frequency of certain SNPs.

The scope for these studies, predictably, mirrors the expansiveness of the human genome itself. In order to find truly significant associations between certain SNPs and disease incidence, the studies require an enormous amount of significant power. This is accomplished through extremely large sample sizes, numbering in the tens of thousands, and strict statistical thresholds for significance, with a p value of 10⁻⁸ as an often-used point of difference.⁶ But scales of this study inevitably present the logistical difficulties of obtaining an appropriately balanced and large enough sample population. Furthermore, there also exists a “Faustian bargain” between studying extremely large case-control populations and considering gene-environment effects.⁸ Studies which utilize extremely large case-control populations, without controlling for multiple environmental exposures, are useful only for finding variations in pathways that function independently of the environment. Given the wide range of environmental exposures potentially within the study population, these large-scale GWAS may conceal important causal pathways dependent on gene-environment interaction, which have been shown to be integral in progression of multiple diseases, such as asthma and allergy.⁸

One example of how GWAS has been applied is the recent research into the genetic basis of Systemic Lupus Erythematosus (SLE). Given the wide clinical heterogeneity seen among patients, and the effects which the disease has on multiple systems of the body, SLE has emerged as a candidate disease upon which the principles of GWAS can be used to ascertain the variations potentially related to disease onset. As such, researchers in the field have placed much promise upon the use of GWAS to elucidate its causal pathways and reveal potential methods of treatment.

GWAS & SLE

SLE is a genetic disease characterized by significant production of auto-antibodies in multiple organ systems, most often in the form of anti-DNA antibodies, and an accumulation of auto-antibody-auto-antigen immune complexes, often leading to an inflammatory response and tissue damage.⁹ Within the past two years, a multitude of genome-wide association studies have expanded the number of candidate susceptibility loci, from nine in 2007, to currently more than 20 loci that show significant association with SLE onset.⁹ The discoveries have shed light on the potential causality of SLE as well as the applicability of GWAS in assessing complex diseases, in

general. In many cases, GWAS has reaffirmed findings found in traditional linkage studies, such as the link between disease onset to variation in regions encoding proteins related to the major histocompatibility complex (MHC) and interferon production. But it is the novel genetic loci, discovered by recent GWAS, which have garnered attention within the research literature. These newly discovered associations have linked SLE to the function of the complement system, B and T cell activation, and apoptosis, among other systems.

Yet, as with all GWAS studies, the identification of association does not indicate causality. Genes within the HLA region have exhibited strong association with SLE through multiple GWAS, but the difficulty upon identification of candidate genes lies in identifying the causal pathway by which HLA function may affect SLE onset.¹⁰ With such a clinical heterogeneity evident in SLE patients, the presence of multiple contributing variations at one or two loci within the HLA region may confound the ability to fully determine the exact contribution of the HLA region to SLE pathology. Determining the close association between SLE and regions with highly specific functions, however, may suggest potential specific explanatory pathways.

One such association is a functional polymorphism identified within the PTPN22 gene, which encodes for an intracellular protein tyrosine phosphatase called Lyp. The R620W polymorphism, which is an arginine to tryptophan substitution, disrupts the binding of Lyp to the SH3 domain of Csk, which is a suppressor of T-cell signaling.¹⁰ Thus, such a polymorphism could disable T-cell suppression and contribute to over-activated T cells and autoimmunity seen within SLE. The finding of this polymorphism is an example of how GWAS can be supplemented with additional experimental data to suggest a biochemical pathway, from variation to disease. It is also likely, however, that a polymorphism such as R620W, on the basis of its specificity, would have a much larger effect size than one affecting the broader HLA pathway.

Where GWAS may prove most useful, however, is linking SLE with systems rather than specific genes. GWAS have identified multiple genetics hits for polymorphisms in regions encoding for proteins related to the complement system (ITGAM/Complement Receptor 3 and C1q complex proteins) as well as B cell activation (BLK and BANK1).^{9,10,11} While fleshing out the biochemical pathways for each of the individual genes may prove useful to identify their function in SLE, these findings have instant real-world applicability in that they can suggest potential novel therapeutic options in treating SLE by addressing the system affected. Indeed, researchers have suggested that symptoms of SLE may arise as a result of the inability of the complement system to clear dead cells or immune complexes, thus leading to inflammation and autoimmunity.⁹ Identifying multiple genetic associations between SLE and the region encoding complement proteins, solidifies this hypothesis, and provides the justification for directly addressing the complement system in SLE therapy. One interesting additional point to note, is that a large amount of autoimmune disease show a clustering of polymorphisms around the same loci, indicating that similar systems and causal pathways may contribute to each disease.¹²

Thus, identification of these systems in SLE research could have repercussive impacts on the analysis of other diseases.

GWAS: HERE TO STAY?

With a multitude of genome sequencing centers and millions in funding going towards GWAS and related studies, it does indeed appear as if GWAS will play a significant role in the future of disease-related research. Yet the optimism of scientific discovery must be checked by the realization that GWAS, and identifying candidate loci, is only the first step towards truly unearthing causal pathways for complex diseases. In order for full realization of findings made from GWAS, this data must be supplemented with laboratory and clinical studies. In addition, significant gains must be made in obtaining appropriate study populations, which ensure both validity as well as repeatability of findings. One concern to note currently is that the majority of studies conducted with GWAS have focused upon white European study subjects, with several additional studies suggesting that the lower degree of linkage disequilibrium in Africans and geographically-isolated populations may limit the efficiency of GWAS in these populations. As with much genetics research, the findings discovered via GWAS are likely to put forth a variety of ethical questions. Realization of the full research potential of GWAS would necessitate research upon populations of various ethnic backgrounds. As these methodological issues are addressed, however, and technological advances are made in improving experimental efficiency, GWAS has the potential to be a breakthrough tool in disease research.

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The Role of Oxytocin in Impaired Social Cognition in Autism Spectrum Disorders

John J. Salvatore

Autism spectrum disorder (ASD) is an umbrella term that encompasses the diagnoses of Asperger's disorder and pervasive developmental disorder-not otherwise specified, in addition to the more severe diagnosis of autism. Interest in the causes and treatment of ASD has spiked in recent years due to an increase in prevalence in ASD in children over the last decade, to approximately 3.4 per 1000 children.¹

Although the causes of ASD are not yet fully understood, a controversial hypothesis that measles-mumps-rubella (MMR) vaccine and thimerosal-containing vaccines cause autism was definitively ruled out by a 2004 Immunization Safety Review.² There is much stronger scientific evidence implicating a role of genetics in the development of the disorder; one study determined the heritability of autistic disorders to be around 90%.³ Genome-wide searches for loci that convey risk for ASD have produced candidate genes on nearly every chromosome,⁴ though the genetic basis of ASD remains ambiguous and elusive.⁵

One of the most debilitating impairments that ASD patients must cope with is the development of abnormal social cognition. Research conducted in animals suggests that the uniquely mammalian hormone and neuropeptide oxytocin plays a key role in the development of normal social cognition and behavior in a multitude of species. The aim of this review is to examine studies conducted in nonhuman mammals, as well as recent genomic studies and clinical trials to investigate whether an abnormal oxytocin system may contribute to the development of impaired social cognition in ASD.

Oxytocin injections into the left lateral ventricle of female rats have been shown to cause the full expression of maternal behavior.⁶ The onset of normal maternal behaviors in female rats following pregnancy was blocked when oxytocin receptor antagonists were infused.⁷ One research team found that patterns of oxytocin receptor density in several brain areas of prairie voles predicted maternal behavior⁸ and that blocking these receptors with oxytocin antagonists eliminated spontaneous maternal behavior. Interestingly, one study reported that maternal behavior in rats was highly heritable across generations, but was not attributable to differences in genotype.⁹ A subsequent study found that these differences in maternal behavior were associated with differences in oxytocin receptor expression in the central nucleus of the amygdala,¹⁰ a structure thought to be heavily involved in processing emotional content. Studies of postpartum human mothers found that oxytocin levels were correlated with a mental component of human bonding, including attachment-related thoughts and frequent checking of the child.¹¹

Other studies found that infant oxytocin receptor knockout mice showed deficits in social discrimination,¹² as did

infant oxytocin knockout mice.¹³ Infusion of oxytocin in adult male rats was found to double the time spent in physical contact with females.¹⁴ Brain infusions of oxytocin were found to initiate the formation of pair bonds in prairie voles, whereas oxytocin antagonists administered at the same time eliminated the formation of pair bonding.¹⁵ A recently published study found that female prairie voles treated with nucleus accumbens infusions of adeno-associated viral vectors containing gene coding the oxytocin receptor resulted in a local increase in receptor expression and also accelerated the development of partner preferences.¹⁶ Studies in primates have shown that highly social bonnet macaques have high oxytocin levels, whereas socially withdrawn pigtail macaques show lower levels.¹⁷ In humans, double blind administration of intranasal oxytocin prevented subjects from reducing trust of others in the face of betrayal.¹⁸ Additionally, participants who received oxytocin showed reduced brain activity measured by functional magnetic resonance imaging (fMRI) in the amygdala.¹⁸

Oxytocin administration has also been shown to facilitate social memory and recognition among rats.¹⁹ Male oxytocin knockout mice were found to exhibit symptoms of social amnesia, but social memory was completely restored after brain infusion of oxytocin.²⁰ Intranasal administration of oxytocin also improved humans' recognition of previously presented faces.²¹

Another study found that intranasal administration of oxytocin was effective in reducing the number and severity of repetitive behaviors over a four hour period in human patients diagnosed with ASD.²² Recent studies have found that oxytocin administered intranasally was effective in improving the processing of emotional cues conveyed by faces²³ and of emotional content of speech²⁴ in patients diagnosed with ASD.

Three separate studies examining differences in single-locus alleles and haplotype frequencies between patients with ASD and healthy controls have found single nucleotide polymorphisms (SNPs) and haplotypes conveying heightened risk for autism within the 3p25 region, containing the gene for the oxytocin receptor.^{25,26,27} One remarkable study found evidence of an epigenetic inheritance due to significant increases in methylation within the promoter region of the gene coding for the oxytocin receptor in ASD patients compared to healthy controls.²⁸ This hypermethylation was correlated with decreases in oxytocin receptor expression.²⁸

These studies suggest that the oxytocin system is heavily involved in the expression of normal social behaviors, including maternal behavior, pair bonding, and social memory

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across several species of mammals. The findings from animal studies have received support from research done in humans linking oxytocin levels to socially relevant variables, such as attachment-related thoughts and trusting behavior.

The oxytocin system likely mediates social cognition via the brain's reward and pleasure system, as increasing the expression of oxytocin receptors in the nucleus accumbens, an area heavily involved in addiction and rewarding behaviors, facilitated pair bonding. The amygdala is also a likely locus of oxytocinergic influence, as it has been linked to social cognition in both in animal and human studies. In humans, the influence of oxytocin on the amygdala may be the basis for emotional processing of socially relevant stimuli.

The findings that intranasal oxytocin administration alleviated deficits in emotional processing as well as repetitive behaviors, two of the most characteristic symptoms of ASD, suggest that an abnormality in the normal brain oxytocin system may underlie the disorder. This claim has recently found support from the genomic literature reviewed linking ASD to hypermethylation of the promoter region of the gene encoding the oxytocin receptor. These results also reconcile the disparity between the high heritability of ASD and the lack of genetic evidence to support it. Considering the evidence for an epigenetic mode of inheritance of maternal behavior in rats, it seems plausible that a similar epigenetic mode of inheritance may underlie ASD.

Although the etiology of ASD still largely remains a mystery, recent evidence has begun to shed some light on the issue. Converging evidence across multiple disciplines, including neuroendocrinology, genomics, molecular psychiatry, and other biomedical sciences suggest that the brain oxytocin system may underlie the abnormalities in social cognition characteristic of ASD. Although ASD shows high heritability, the disorder likely has an epigenetic rather than purely genetic basis. The oxytocin system may prove to be a fruitful target for researchers and physicians seeking novel treatments to improve the lives of both ASD patients and their families.

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